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THE UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANISATION

SUCH accounts of the proceedings of the General Conference of the United Nations Educational, Scientific and Cultural Organisation held in Paris last September as are yet available in Britain indicate that the Organisation has been brought to face the question as to the real value given for its expenditure, estimated at almost nine million dollars for the current year. Of this sum, two million dollars is for general administration, one million for education, nearly two millions for communications, more than 800,000 for the natural sciences, more than 450,000 for the social sciences and 400,000 dollars for the reconstruction programme. The United States and Great Britain supply something more than half the income, the rest being made up by the British Commonwealth, including India, the countries of Western Union, Denmark, Norway, Switzerland, with small contributions from Afghanistan, Austria, the Lebanon, Liberia, the Philippines, Thailand and Venezuela.

In commenting on the Director-General's report on September 21, Mr. D. R. Hardman, leader of the British delegation, made a strong plea for Unesco to cut its expenditure and concentrate its efforts on essential projects, and to temper its idealism with the realism of hard facts. His speech reflected a trend of opinion on the future of Unesco which seems to be fairly general among member-States who pay their subscriptions to Unesco as against that among the twenty-six members of the Organisation who do not pay. The latter are pressing for more expenditure, whereas the school of thought to which Mr. Hardman gave expression holds that the programme is still too widespread and diffuse, and that by concentrating on activities likely to yield the most tangible results, Unesco should not only become effective, but should also be run more economically.

The matter is obviously of more than academic interest for Britain. The Director-General, Dr. Torres Bodet, is willing to concentrate Unesco's activities; but he points out rightly that the programme was determined not by the secretariat but by the General Conference at Beirut last year. He is reluctant to jettison the less urgent activities and is naturally concerned lest education, culture and science should become the Cinderellas of the United Nations specialized agencies. The Organisation is not, in truth, a wealthy organisation, and the extra million dollars sought by the Director-General is not, relatively, a large sum. The real question is whether Unesco is the best agent for disposing of a new largess from the United States and Great Britain for such ends, or whether more appropriate means exist in some other organisation.

Some such reflexions may be induced by the choice by the Director-General, in consequence of a resolution passed at the second General Conference of the Organisation at Mexico City in 1947, of "Food and People" as a single topic for group discussions in 1949 on the social and international implications of science.

The campaign on "Food and People" was, indeed, Unesco's most rewarded effort of the year in Britain, and the discussions emphasize the value of the Organisation's contribution towards the educational campaign which must accompany the application of science to agriculture and problems of human nutrition. The difficulties which have been encountered in dealing with the swollen shoot disease of cacao trees in West Africa have emphasized the importance of this factor. This was fully appreciated by the United Nations Scientific Conference on the Conservation and Utilization of Resources recently held at Lake Success. In a review of the work of that Conference, Sir Harold Hartley has pointed out that the provision of the factual background for the work of the Economic and Social Council in implementing President Truman's Fourth Point raises important problems of collecting and co-ordinating the results of surveys as well as in initiating the actual surveys. He visualized the need for some body to act as a liaison in technical problems between the specialized agencies of the United Nations.

Other thinking on similar lines has raised the whole question of the purpose of the United Nations Educational, Scientific and Cultural Organisation, and whether or not it should become essentially an information agency for the United Nations. For example, in a recent article in *Foreign Affairs* entitled "Yardstick for Unesco", the managing editor, Mr. Byrom Dexter, after rejecting the latter idea, suggested that the support the Organisation can bring to the United Nations should be the criterion for measuring its work. The United Nations has already a satisfactory information service, and Mr. Dexter thinks that Unesco should address itself explicitly to the co-ordination of the organs and agencies of the United Nations. This is the central problem of world co-operation, and Mr. Dexter insists that the Organisation must recognize that it cannot avoid political action and must seek deliberately to become an effective instrument of internationalism. In his view, the future of a cultural organisation such as Unesco lies in building up a sense of world community, in which public opinion will be sufficiently informed and alert to take a world point of view, and support decisions of the major organs of the United Nations in any time of emergency.

That is one point of view. Mr. Dexter says little or nothing of particular projects. At the recent Paris meeting, however, Mr. Hardman noted the enormous output of memoranda and documents, amounting to 30 million pages, coming from the Organisation in the past year, and suggested that Unesco should make full use of the expert publishing machinery which already exists in some countries rather than attempt to set up a publishing house of its own.

Various documents fortunately are now available for an independent appraisal. Besides the Director-General's report, there is the "Report of the United Kingdom to Unesco for the Year 1949", issued by the Minister of Education; this survey of the activities of the United Kingdom National Commission gives an indirect picture of the activities of the Organisation. Even documents dealing with limited topics, such as the final act of the International Conference on Science Abstracting, convened by the Organisation in Paris last June, and the long memorandum from the Organisation contained in a recent report from the United Nations on "The Question of Establishing United Nations Research Laboratories", afford material for study in the same context.

In presenting his estimates to the General Conference, Dr. Bodet referred particularly to the establishment of an International Institute of the Arid Zones. This, as well as the joint undertaking, with the World Health Organisation, to create a Council of Medical Sciences, the support of the International Union for the Protection of Nature and maintenance of the work of the field science co-operation offices, demand increasing funds, as would the requests for help from the social sciences. Stress was also laid by the Director-General on the value of the programme for the exchange of persons and on the desirability of increasing the number of Unesco fellowships.

In determining his own priorities as regards the two-year programme for the Organisation adopted by the General Conference at Beirut last year, the Secretary-General was guided by the practical value of particular projects in raising the standard of living of ordinary people, their likelihood of securing the co-operation of leading intellectuals and professional people and the probability of quick and tangible results. He agrees that the Organisation must concentrate on certain practical tasks which it can complete with the resources at its disposal, and the value and meaning of which are beyond all doubt. The Code of Eighteen Directives submitted to the General Conference for adoption as basic principles of Unesco should also assist in giving a more concrete shape to its activities, although they will not eliminate the need for clear thinking, close scrutiny and criticism of individual projects from within the Organisation itself, by the national commissions and by the professional organisations concerned.

The importance of this last point is well brought out by the fact that a number of the projects before the United Nations Educational, Scientific and Cultural Organisation make considerable demands on the world's resources of scientific and technical manpower at a time when even such countries as the United States and Great Britain are finding their own plans for development restricted by the insufficient supply of such men and women. The Abstracting Conference already mentioned, and also the proposal for United Nations research laboratories, have both to be considered in this context.

The Science Abstracting Conference is only one among many activities of the United Nations Educational, Scientific and Cultural Organisation, but the "Final Act" of the Conference does display some of its characteristic weaknesses. The Organisation can set forth admirably and in detail what is required in theory; but out of the many tasks inviting attention it can rarely differentiate those which are most urgent, for which resources are immediately

available and which on practical grounds should receive prior attention. It can define the final objective, but can seldom formulate a project the execution of which is immediately practicable. This inherent weakness is due primarily to Unesco's wide terms of reference, but partly also to disproportion between the plans of the Unesco secretariat—a full-time professional staff—and the capacity for execution of the national voluntary bodies on whom the responsibility for action largely falls.

This is again brought out by the report of the Minister for Education noted earlier. While the Minister of Education is responsible for the United Kingdom policy towards the United Nations Educational, Scientific and Cultural Organisation, and his staff provides a small secretariat for Unesco interests, the detailed work on such projects is done by groups of specialists, known as "national co-operating bodies". The Royal Society, for example, has established a British committee for co-operating with Unesco in the natural sciences, and the Committee of Vice-Chancellors and Principals assists in nominating members of the Universities Group. The work of the national commissions is, in fact, based on voluntary effort, and there are limits to the amount of time which their members can place directly or indirectly at the disposal of Unesco.

The general debate at the Paris Conference showed that the work of Unesco which is most appreciated is that done in simple educational campaigns at a practical level. There was widespread gratitude for the ingenious book-coupon scheme by which 'soft-currency' countries can get 'hard-currency' books. Educational missions, the supply of text-books and translations, assistance to adult education, and measures to raise the educational standards in semi-illiterate countries or among refugees were demanded and appreciated.

All this indicates the soundness and the importance of Unesco's ideas on fundamental education, and it is in the same connexion that the United Nations has asked the Organisation to participate with other specialized agencies in plans for technical assistance to undeveloped areas. The idea of United Nations research laboratories is not specifically a Unesco project. The Organisation contributed the largest and most detailed reply to the Secretary-General's inquiry, and included some specific proposals which have since been elaborated in greater detail in the United States by the National Research Council Committee on Unesco. The latter Committee itself was in favour of the immediate establishment of an International Computation Centre, a United Nations Institute of Human Sciences, and, under the joint auspices of Unesco and the World Health Organisation, of an Institute of Geo-medicine. All these proposals were considered in August by a Committee of Scientific Experts, whose eight members included Dr. J. Needham and A. T. M. Wilson of Great Britain, and Dr. Harlow Shapley and Dr. R. Likert of the United States. Their official report has yet to appear; but it seems clear that once again, if the Organisation is to act for the United Nations in this matter, it will be required to do so in close co-operation with other specialized agencies as well as with the national co-operating bodies. That may be an added reason for Unesco taking up, as Mr. Dexter suggested in *Foreign Affairs*, the study of international organisation. It is likewise an imperative reason why the central secretariat and the whole planning of Unesco projects should be brought, through the national commissions, into the closest possible touch with those national bodies on whom so much of the responsibility for execution must fall. It is important, too, that the Unesco secretariat should understand more clearly the limitations which considerations of national resources of men and materials may place on the contribution to new international institutions.

The Director-General's report shows that he clearly recognizes the importance of such contacts between the secretariat and the national commissions and co-operating bodies, as well as with governments and the other specialized agencies of the United Nations. In the scientific field, however, there must be much fuller and more widespread knowledge, and a clearer understanding, of the work and nature of Unesco among scientific workers themselves. They must supply some of the creative thought essential to shape policies and plans which can be executed with the resources at our disposal to-day. Idealism will always supply something of the driving force; but it must be tempered by a practical realism. Some of the material has been indicated above from which such thinking could start, not only to inspire practical programmes but also to shape an effective organisation in which Unesco might play its appropriate part by focusing attention successively on growing points or problems demanding for their solution the co-operation of several countries. Having defined the problem, inspired the initial attack and mobilization of the necessary resources, Unesco would leave it to the appropriate bodies in co-operation to carry the project to completion, while the Organisation itself would pass to the consideration of other problems requiring attention at the international level.

ENCYCLOPÆDIA OF CHEMICAL TECHNOLOGY

Encyclopædia of Chemical Technology
Edited by Raymond E. Kirk and Donald O. Othmer. Vol. 1: A to Anthrimides. Pp. xxiv+982. 20 dollars. Vol. 2: Anthrone to Carbon-Arc. Pp. xvi+915. 20 dollars. (New York and London: Interscience Publishers, Inc.)

THESE two volumes of nearly a thousand pages each are the first of a projected series of ten volumes, two to three volumes being due each year. The object of the series is to provide an up-to-date survey of the field of chemical technology, partly as a work of reference for chemists and chemical engineers working in industry, and partly as an aid in training students in modern technology. A large number of separate articles, written by specialists in the several fields, are presented in these two volumes; many chemical compounds are included, with extensive data on their physical and chemical properties

and indications as to applications and processes of industrial manufacture. These articles are of interest not only to the technologist but also to the academic chemist, since they show the relation between the substances which they normally use in the laboratory with the wider world of technology. Care has been taken to use nomenclature which provides easy reference. A bibliography relative to each main item is given. There is also information about manufacturing costs and methods of packing materials for transport; these may not, however, be applicable outside the United States. This reservation applies also to the description of aluminium alloys, which are referred to by their code names.

The aim of the "Encyclopædia" to be up to date is generally reached. The section dealing with analysis, for example, is very satisfactory; an omission noted is that there is no mention of the determination of oxygen by magnetic methods—perhaps it will be mentioned in a later volume under gas analysis. The article draws a useful distinction between accuracy and precision, and also between a quantitative determination and the greater problem of making such a determination possible. The articles are well presented and readable.

There are some statements which without further exposition could lead to misconception; for example, that on p. 535 "that a reaction can take place only if there is a decrease in the free energy between the starting materials and the final products". Some indication of the scope of the "Encyclopædia" is given by the following selection of topics: antianæmia preparations, antibiotics, antifreezes, antioxidants, antiscorbutics and antiseptics. Many of the articles are worth reading as general surveys of particular fields, and the detailed information which they contain is useful for reference. The technologist will be interested in the articles on asbestos, asphalts and various bituminous materials, baking and beer. Those interested in medical matters will find a lengthy description of the technique of blood fractionation, while for the chemist, the sections, for example, which deal with carbon arcs, modern methods of calorimetry, butadiene, benzoyl peroxide, azo-dyes and antioxidants are of interest. Among the many illustrations is a graph which shows that the price of ascorbic acid has decreased steadily since 1937—encouraging in these days of rising costs. If future volumes maintain the standard set by Volumes 1 and 2, the complete series should be a particularly useful addition to libraries. A. C. EGERTON

COSMIC RAYS, MESONS AND NUCLEAR DISINTEGRATION

Cosmic Radiation

Colston Papers based on a Symposium promoted by the Colston Research Society and the University of Bristol in September 1948. Pp. viii+189. (London: Butterworth's Scientific Publications; New York: Interscience Publishers, Inc., 1949.) 25*s*. net.

THE Colston Research Society is a body of citizens of Bristol and members of its University, which at its foundation fifty years ago had the aim of aiding the development of the University College into a full University; since then, it has assisted research over the whole range of studies in the University. This task having now become so great that the burden must be shouldered more and more by government funds, the Society has adopted a new policy of devoting its resources to the promotion of annual symposia at the University. The present volume contains the contributions to the first of these symposia.

The subject, cosmic radiation, was particularly suitable for the occasion, because it has been developing with exceptional rapidity in recent years, largely as the result of a new method of investigation the potentialities of which were first fully understood and exploited by Prof. C. F. Powell and his collaborators at the University of Bristol. This method consists in the use of photographic emulsions for the recording and study of nuclear processes. Special emulsions have been developed for the purpose as a result of experience, in which the gelatine contains not only silver halide grains but also other atoms such as boron. Packs of photographic plates are specially useful for studies at very high altitudes, because of their small weight, simplicity, large stopping-power and continuous sensitivity. The silver halide grains are made developable by ionization produced by charged particles passing through the emulsion. When a cosmic-ray particle hits a nucleus in the emulsion, so as to produce a nuclear explosion, the tracks of the issuing particles are made visible by development of the plates and by the piecing-together of strips of emulsion from different plates of the pack; this gives a wealth of detailed information as to the event and its products. The emulsion technique now takes its place with the Wilson cloud chamber and Geiger Müller counter methods as a leading instrument of attack on the problems of cosmic rays and nuclear physics.

The volume contains thirty contributions from laboratories in many countries. Their subjects are too numerous to describe even in outline; among the principal new results mentioned are the following. It is found that the primary cosmic rays include not only the nuclei of hydrogen (mainly protons) and helium, but also a very small proportion of heavier nuclei, with atomic numbers between those of carbon and iron; this fact is thought to favour the hypothesis that cosmic rays are produced by some process of adiabatic acceleration, perhaps in regions of changing stellar magnetic fields, rather than by some catastrophic process. Another recent major discovery now being developed is that there are several different kinds of meson, such as σ and ρ, π and μ, the mass ratios and charge relationships of which are becoming clear. These mesons can now be produced and studied in the cyclotron. Several papers deal with the effects of the absorption, in a nucleus, of different types of primary cosmic-ray particle or meson, and the consequent re-distribution of energy inside the close-packed nucleus. This leads to the emission of protons and neutrons by a process akin to evaporation; also of alpha-particles, which mostly escape with energies well below the potential barrier of the nucleus. When the incoming particle has exceptionally high energy, some of the emitted particles seem to be directly 'knocked-on', and in some cases nuclear fission may occur.

Prof. R. Fürth gives a theoretical deduction of the mass ratios of π- and μ-mesons and electrons (m_e) and protons (m_p), seemingly in good agreement with the best measurements: his theory gives $m_p/m_\pi = 2\pi$ or $m_\pi/m_e = 293$ as compared with the experimental value 260 ± 30; and $m_\pi/m_\mu = 1 + 1/\pi = 1{\cdot}32$, as compared with the experimental $1{\cdot}33 \pm 0{\cdot}05$.

WAR-TIME TECHNOLOGY IN THE UNITED STATES

Q.E.D.: M.I.T. in World War II

By John Burchard. Pp. xvi + 354 + 16 plates. (New York: John Wiley and Sons, Inc.: London: Chapman and Hall, Ltd., 1948.) 21*s.* net.

Battlefronts of Industry

Westinghouse in World War II. By David O. Woodbury. Pp. ix + 342 + 32 plates. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1948.) 21*s.* net.

THESE two books, one the story of the Massachusetts Institute of Technology in the Second World War and the other that of the contribution of the Westinghouse Electric Corporation to the victory over the Axis powers, reveal the enormous achievements made by civilian forces during the War. The Massachusetts record "Q.E.D." is that of the assistance given to the war effort by a single privately endowed American institution, and is typical of the war-time contribution of the academic institutions. The author rightly points out that his book is not the history of the achievements of individuals, because research and development in these days are almost always the work of teams. Indeed, throughout, one quality of the war-time activity of the Institute stands out clearly—the quality of unity and simplicity. However difficult and numerous were the problems, there was always just one criterion for their solution: "Is this the most useful thing which M.I.T. can do to help win the War?"; and when this question had been answered, all its powers and activities were organised to this end.

In a foreword to the volume, the president, Karl T. Compton, says that one of the outstanding lessons of the War was the great value of civilian experts at high levels in the military and other government councils. Civilian pressure broke down peace-time routine. It was civilian pressure which opened the way for the training of thousands of radar experts; which convinced those in high authority that the traditional methods of anti-submarine warfare were inadequate; which developed the amphibious 'DUKW', in spite of lack of interest by the military authorities, and similarly the rocket missiles. The war-time contribution of the Massachusetts Institute of Technology falls into three categories: (1) research and development contracts; (2) special training courses; and (3) personal service by its staff. The range of technical problems undertaken by the personnel resources, past and present, of this great institution was enormous, and the author of "Q.E.D.", John Burchard, director of libraries at the Institute, has with superlative skill made a most fascinating story.

"Battlefronts of Industry", the record of the Westinghouse Electric Corporation of its activities in the War, is written in a popular style and well illustrated, and shows in a striking way the American genius for quick production on a large scale. It shows how the policy determined by the expert management was developed by the research and engineering staffs and then carried into effect with the full weight of a great manufacturing organisation behind it. An early decision of the management to embark only on those war projects which would lend themselves to future peace-time production was soon abandoned when the full needs of the Armed Forces became increasingly recognized. The range of activity undertaken by the Corporation was enormous, in both size and complexity, and emphasizes this important lesson to be learned from the War, namely, that unless a country possesses a weight of manufacturing resources backed by free initiative and enterprise, it will suffer a great handicap when its normal productivity has to be geared to war effort. Among the most interesting of the twenty-four chapters of the book are those on "The Impossible takes a Little Longer", "Uranium" and "The Battle of the Isotopes".

The student of the history of the War will do well to study these two volumes, bringing out, as they do, the inception of new ideas and the effort required to translate these into war devices.

A. P. M. FLEMING

ULTRA-HIGH FREQUENCY RADIO FOR STUDENTS

Ultra-high Frequency Transmission and Radiation

By Nathan Marchand. Pp. ix+322. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1947.) 27*s.* net.

THE Second World War and the succeeding years have seen a great extension of the use of radio waves of very high frequency, largely as a result of the stimulus provided by the development of radar, and of television and frequency-modulation broadcasting systems. It is therefore perhaps not surprising that there have appeared recently several books on matters associated with the use of such short waves. However, it might be suggested that the time has now been reached when intending authors and publishers in this field should consider carefully what they have to offer before adding to the list. One might particularly emphasize that it seems scarcely necessary nowadays to include a treatment of vector analysis, and a detailed derivation of Maxwell's equations, together with the fundamental principles underlying electromagnetic radiation, in every new text dealing with very high frequency radio phenomena.

The headings of the eight chapters in the present book are as follows: transmission lines, elements of vector analysis, fundamental electromagnetic equations, plane electromagnetic waves, radiation, antenna arrays, wave guides, and complex transmission-line network analysis. It is the reviewer's opinion that, unless an author has some essentially new points of view on these subjects to present—and such are not evident in this book—there would appear to be little justification for producing a further treatment.

Mr. N. Marchand states in his preface that he has "prepared this book keeping in mind the requirements of both the college student who will study it as a textbook in a prepared course, and the practising engineer who will read it for self-instruction". Nevertheless, although there is little to quarrel with in the manner of presentation of the material, it is a little difficult to see what the student or engineer will find in this book that is not already covered adequately in several well-established texts on physics and electrical engineering. This criticism is supported by the numerous references to such books as those, for example, by Stratton and Schelkunoff. There are included a number of tables; but these also are such as one would expect to find in any of the widely available collections of mathematical tables.

J. A. SAXTON

NEW EVIDENCE ON THE MODE OF ACTION OF 'MITOTIC POISONS'

By ANTHONY LOVELESS and STANLEY REVELL

Chester Beatty Research Institute, Royal Cancer Hospital, London, S.W.3

I. Biology

IN 1925 A. P. Dustin[1] reported that certain chemical agents which he called "*poisons caryoclasiques*" were able to exert a toxic action on cell nuclei without apparently injuring the cytoplasm. It has since been claimed that a wide variety of compounds can act in this way (see, for example, reviews by Dustin[2] and Astaldi *et al.*[3]), and, since they appear to be active only on dividing cells, they have sometimes been called mitotic poisons.

Broadly speaking, the problem has been attacked from two main positions. The medical discipline, with the question of cancer therapeutics in mind, has usually chosen as its experimental material mitotically active animal tissue, either *in vivo*, as, for example, in studies of the intestinal crypts of Lieberkühn, or *in vitro*, as in work on chick fibroblasts. Empirical observations on cell effects and measurements of the growth inhibition of the tissue or tissue culture have been used as criteria for the activity of the agent under test. Geneticists and cytologists, on the other hand, have in recent years worked on quite a different line. By the use of the precise techniques that had previously been devised for the detection and quantitative estimation of X-ray effects, they have shown that certain classes of these compounds likewise are mutagenic agents, for they can cause heritable nuclear changes that are demonstrably similar to those induced by X-rays. Consequently they have used as experimental materials those, such as *Drosophila* and the classical cytological objects, which were best suited to the application of these techniques; and they have felt justified in doing this by their confidence that their results could in general be extrapolated to other cellular systems.

It has therefore come about that workers with training and research experience in these widely different fields have contributed to what is now an extensive literature. Compounds have been reported as 'active' on different criteria, on different materials, and under entirely different test conditions. Some workers may even disagree as to what results should be included as comparable at all. Nevertheless, the object of the present article is to evaluate a few of the different methods and results and to attempt to correlate the chemistry and modes of action of certain of the different classes of compounds that have been used. The article is thus designedly critical and selective and is not intended as a comprehensive review.

The observed effects of the compounds reported as active have been divided into three categories. The first includes those compounds which have been shown by genetical or cytological test to be radiomimetic. All the work in this field stems from Auerbach's original discovery that by the *ClB* test mustard gas, like X-rays, is mutagenic[4]. Mainly from the work of Auerbach, Robson, Carr, Koller and the Slizynskis[5], both nitrogen and sulphur mustards are now known to cause gene mutation and chromosome breakage. Other compounds which it is claimed induce either gene or chromosome changes, or both, include allyl *iso*-thiocyanate[6], urethane[7], phenol[8], certain of the aminostilbenes[9], formaldehyde[10], 20-methylcholanthrene, 3 : 4-benzpyrene, 1 : 2 : 5 : 6-dibenzanthracene and β-naphthylamine[11].

These compounds are of interest not because of any direct toxic effects they may produce in the cell during their presence there, but because of the irreversible hereditary changes they induce in the nucleus. These hereditary changes or mutations will persist after the agent itself has been lost or destroyed, and at the subsequent mitosis will cause a loss or an asymmetric segregation of genetic material. The two daughter nuclei of this mitosis will have a deficient or unbalanced genetic complement: cells so affected will either die or will at least have a reduced viability.

Although these agents are said to be radiomimetic, it is of vital interest, from the point of view of their mode of action, to determine whether this is strictly true: whether the type and incidence of the heritable change that they induce is exactly that which is also induced by X-rays. Several differences have already been found. Auerbach has shown in her mustard gas experiments with *Drosophila* that in the progeny of a treated individual the frequency of mosaicism is very high—as much as 50 per cent of observable mutation being of this type. Thus the change induced may not manifest itself phenotypically for several cell generations at least. Such mosaics occur after X-ray treatment, though the incidence is relatively small. The *Drosophila* results also show that after mustard gas treatment the number of observed chromosome translocations is smaller per number of sex-linked lethals than after X-irradiation.

Auerbach's results do not, however, indicate that mustard gas has any selective action on the chromosomes. But Ford[12] working with a nitrogen mustard, NN-di(2-chloroethyl)methylamine, has shown that in *Vicia* root-tip cells the distribution of breaks is very markedly biased towards certain chromosome regions. Ford's work has been confirmed in this laboratory[13], and it has also been shown that these high break regions are certainly very near demonstrable regions of heterochromatin and probably are actually in them, and that the breaks seem to show a proportionality in number that corresponds to the length of the heterochromatic segments. This localization of the breakage is in marked contrast with the more generally distributed breakage that follows X-irradiation. This finding is significant in view of the fact that heterochromatin has a high nucleic acid charge in the resting nucleus, and it is known that the mustards have an affinity for acid groups. We may thus suspect that the extrinsic agent is combining directly with the deoxyribose nucleic acid at the resting stage chromocentres, and that breakage is the result. The cytological effects of di(2 : 3-epoxy-

propyl)ether, the chemistry of which is dealt with later, are precisely the same as those induced by NN-di(2-chloroethyl)methylamine*.

An attempt has been made, again using *Vicia* as test material, to determine where in the nucleus this combination occurs[13]. This work has been based on three premises: first, that the pair of chromosomes carrying the nucleolar organisers are at least partially in the interior of the nucleus; secondly, that the other chromosomes are predominantly disposed on the nuclear membrane; thirdly, that interchange between chromosomes indicates a proximity (in a chromocentre) of these two chromosomes at the time of breakage and reunion. Comparative estimates of the breakage and interchange frequencies in and between different chromosomes following treatment with NN-di(2-chloroethyl)methylamine are quite different from those made on the X-rayed controls, and suggest that combination occurs much more readily with the chromocentres that are on the nuclear surface than with those in the interior of the nucleus. This work will be published in detail elsewhere.

There is no evidence in *Drosophila* of any such selectivity of action; but if the nucleic acid charge and the spatial distribution of the chromosomes within the nucleus are factors influencing the position of breaks, then the nucleus of the sperm and of the plant somatic cell might be expected to react very differently.

A subsidiary group of cytological results have been presented by Cornman[14] on the effects of coumarin and parasorbic acid, by Ostergren[15] on coumarin, and by Levan and Tjio[16] on some phenolic compounds. It appears to us, however, that any chromosome breakage seen after treatment with these compounds is not of the same type as that caused by the mustards, but is due to an induced intercalary stickiness of the chromosomes that leads to the observed anaphase bridges and fragments, an explanation which has, indeed, been suggested by Levan. Kihlman and Levan[17] have published a preliminary report on chromosome breakage induced by caffeine. This result has been qualitatively confirmed by a study of *Vicia* metaphases in this laboratory, but there are at present insufficient data to indicate whether breakage is localized. It should be remembered, however, that the concentration required to produce an observable number of breaks is extremely high, and is of quite another order than that used in the NN-di(2-chloroethyl)methylamine experiments. This suggests that we are here dealing with a different mode of action.

Urethane has been reported as active on plant cells by Oehlkers[7] and has, of course, been used clinically in the treatment of leukæmia. Koller[18] has shown that, after injection into rats implanted with Walker carcinoma, chromosome breakage occurs in the tumour and the bone marrow cells. One positive result obtained after urethane treatment on plant material in this laboratory[13] has, however, proved to be quite irreproducible, and other workers (for example, Ludford and Koller) have also remarked on an unaccountable variation in its activity. With this compound again, relatively high concentrations are required for positive results.

Our second category includes a number of compounds for which activity of a sort has been claimed and which in our opinion require separate consideration. A. P. Dustin[19] described the cytotoxic effects of trypaflavine, and P. Dustin[3] in a review ascribes a trypaflavine-type reaction on mouse intestinal crypt cells to a number of substances including urethane, various cyanates, arsenicals and mercury compounds (as well as hydroquinone and pyrocatechol). A degenerative pycnotic change that appears very shortly after treatment is induced in the nuclei of cells about to undergo division, and since nuclear pycnosis is also one of the immediate effects of X-irradiation Dustin claims that these compounds are radiomimetic. Levan has presented evidence of another kind for hydroquinone and pyrocatechol; but we do not consider Dustin's experiments sufficiently crucial to justify placing the tested compounds in the same class as those shown to be radiomimetic by genetical or cytological test. All available evidence[20] suggests that the truly radiomimetic poisons act on nuclei in the resting stage; consequently their chromosome effects do not manifest themselves until these cells come into division. If the observations are only made at very short intervals after treatment, chromosome breakage will not be seen, for this will only begin to appear to any extent at about eighteen to twenty-four hours. With nitrogen mustards also, as Dustin points out, effects of the trypaflavine type in cells in division can be seen at very early stages after treatment, but these reactions are not of the radiomimetic type which appear at later stages: they are merely an expression of the generally toxic action of all these substances on any tissue and upon rapidly proliferating tissues in particular.

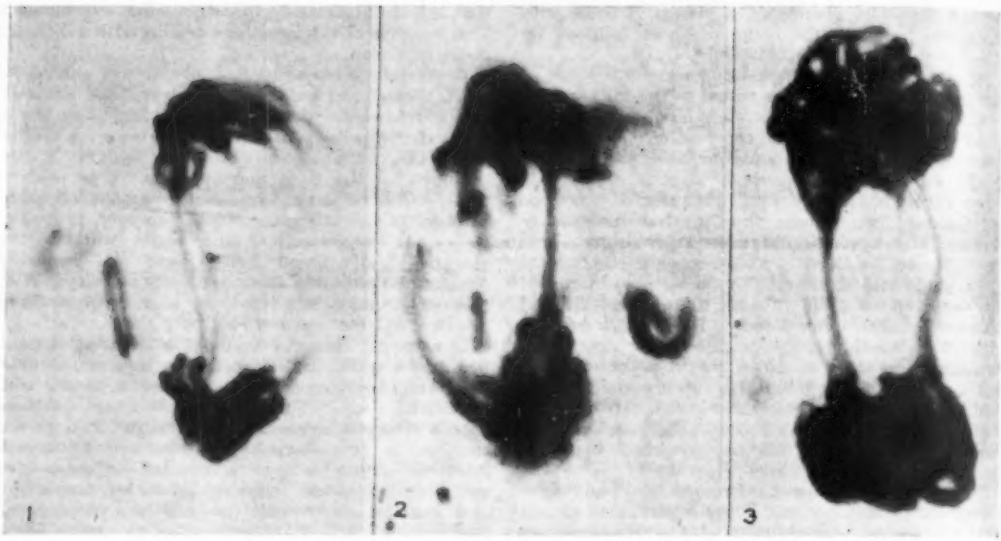
To illustrate this point, Figs. 2 and 3 show cell divisions in root-tip preparations of *Vicia faba* at short intervals after treatment with ethyl alcohol and nitrogen mustard respectively. In both cases division is inhibited and the chromosomes are seen in an adherent condition usually described as stickiness, and there are in the same preparation numerous cells in various stages of the degeneration and pycnosis which follow. The meristems treated with alcohol eventually resumed normal proliferation with no sign that any chromosome rearrangements had been induced. The material treated with nitrogen mustard, re-examined at twenty hours, had also recovered from the general toxic effects of the treatment and was dividing actively; but these divisions showed a high frequency of unequivocal chromosome breaks which at a later stage again completely, and this time permanently, inhibited cell proliferation. The significance of this demonstration is that in both

* Prof. A. Haddow has provided the following note:

(1) In the course of an investigation being conducted here into the mechanism of action of the nitrogen mustards, Dr. W. C. J. Ross of this Institute had originally suggested a series of di-epoxides which it would be desirable to examine, among other types, as biological alkylating agents; this proposal was incorporated in his chemical programme forming part of the investigation as a whole.

(2) Before this suggestion could be put to the test, it reached us again from a different quarter. In connexion with the hypothesis of Goldacre, Loveless and Ross (*Nature*, **163**, 667; 1949), that cross-linking may play an important part in the action of the nitrogen mustards, Prof. J. B. Speakman, of the Department of Textile Industries, University of Leeds, kindly agreed to test a series of halo-alkylarylamines (Haddow, Kon and Ross, *Nature*, **162**, 824; 1948) for their cross-linking potentialities in the reduced keratin fibre. At the same time, Prof. Speakman indicated we should do well to study the biological properties of a number of known cross-linking substances not hitherto so examined, and particularly suggested those di-epoxides which have recently come into prominence as effective cross-linking agents in textile practice. On biological test it at once became evident that a number of di-epoxides, including the di(epoxypropyl)ether referred to in the above text do, in fact produce, in both normal and tumour tissues, effects which are largely indistinguishable from those due to the nitrogen mustards.

(3) Meantime, an independent and contemporary interest in these effects of the di-epoxides had been developed by the Research Department of Imperial Chemical Industries, Ltd. (Dyestuffs Division). By mutual arrangement, separate accounts will be published concurrently at a later stage.



Cells at anaphase of mitosis from *Vicia faba* root-tip preparations. Acetic-alcohol and Feulgen (× 3,000)

(1) Anaphase showing two dicentric bridges and two fragments, after 1 hr. of treatment with $M/10^6$ NN-di(2-chloroethyl)methylamine, and 22 hr. in water. (2) Anaphase showing chromosome lagging and 'stickiness' after 1 hr. of treatment in 1 per cent ethyl alcohol and 2 hr. in water. (3) Anaphase showing chromosome 'stickiness' after 1 hr. of treatment in $M/10^4$ NN-di(2-chloroethyl)methylamine and 5½ hr. in water

cases the initial effects observed indicated that there was a toxic action on the cell but not a genetic alteration in the nucleus.

Toxicity of this type is in itself of interest, but must be regarded as an entirely separate problem. For this reason, in the second part of this paper, where consideration is given to the mode of action of radiomimetic agents, the theory proposed does not attempt to accommodate some of the compounds considered by Dustin to be of the trypaflavine type, since it is not considered that their activity has been substantiated *sensu stricto*.

The last group of compounds includes colchicine and those substances which act in a similar way. Dixon[21] first observed the cytological effects of colchicine on dividing leucocytes. Later A. P. Dustin[22], Ludford[23] and Brues and Cohen[24] studied its effects on various animal tissues. With the discovery by Blakeslee and Avery[25] that colchicine can produce polyploidy in plants, it became apparent that the drug might be of great use to the plant breeder, and much work has since been published on its uses in this direction. Levan[26], in a careful analysis made on *Allium* root-tip cells, showed exactly how colchicine was able to act on the plant cell to inhibit spindle formation, causing the accumulation of metaphases and the formation of polyploid nuclei. Acenaphthene[27] was also found to cause spindle failure and polyploidy in plant tissues. More recently Ostergren and Levan[28] have claimed that a wide variety of compounds can at a critical concentration cause spindle suppression. Ostergren[29] has pointed out that their activity appears to be inversely proportional to their water solubility, and he advances a physical hypothesis for their mode of action similar to that of Meyer and Overton for narcotics. The colchicine-type activity is, however, different from that of the other chemical classes we shall consider, for, although it produces a heritable nuclear change, this change is a quantitative one and is not of the qualitative kind characteristic of the 'radiomimetics': colchicine does not induce gene mutation or chromosome breakage. Any growth-inhibitory action depends first upon its effect in delaying metaphases and so causing a doubling in chromosome number, and secondly, upon the various abnormalities that may arise in the polyploid animal cell at subsequent divisions[30].

In view of the much wider appreciation than hitherto of the important part that induced chromosome changes can play in growth inhibition, we wish to direct attention to the limitations of what we may call the 'bridge and fragment method'. In this type of analysis, anaphases are scored either as normal or as showing a varying number of dicentric and acentric chromosomes. In mammalian tumour tissue and in chick fibroblast cultures, it is impossible to make the necessary detailed observations on the changes in number and morphology of the metaphase chromosomes which, in more favourable material, would be the method adopted to score breakage. The scoring of anaphase effects is thus the only means available. Such an analysis can at best give only an index and never an absolute estimate of the amount of chromosome breakage induced. But it should also be realized that, especially in unfavourable material, the analysis itself requires some experience for its interpretation: the mere observation of disordered anaphases (accompanied perhaps by growth inhibition) is not necessarily an indication that chromosome breakage has occurred. During chromosome segregation at mitosis, the cell performs a mechanical feat which must be, like other cellular functions, a highly organised process. The presence of any extrinsic agent within the mitotic cell may interfere with the division cycle and produce effects that are not easily distinguishable from the effects of breakage and reunion (cf. Figs. 2 and 3 with Fig. 1). Such

tests should therefore be scored with care, and their results accepted with reserve.

II. Chemistry

It appears we must regard the so-called 'mitotic poisons' as comprising at least three distinct classes of compound. Moreover, on examination, each class seems to show a chemical homogeneity correlated with biological activity.

The first consists of a number of compounds well known for some other physiological activity, and these are characterized by their ability to undergo substitution or addition reactions with mercaptans. They include the lachrymators, bacteriostatic and anti-protozoal agents and anti-growth substances of plant origin. They exert a highly toxic, non-specific effect upon the cell and are *non-radiomimetic* in the properly defined sense.

The second class comprises the vesicants such as sulphur and nitrogen mustards, di-epoxides and protoanemonin. Although reaction with —SH compounds has been demonstrated, it is becoming apparent that reaction at other sites, almost certainly acid groups, underlies their important biological effects. Reaction in the case of the mustards is almost entirely by the S_N1 mechanism, which permits alkylation of free amino-groups and anions, and esterification of acid groups is therefore favoured. The value of these compounds lies in the highly specific effect upon the resting nucleus, manifested in subsequent mitosis by the appearance of chromosome breakage and rearrangements of various kinds: for this reason they may be correctly termed 'radiomimetic' and are probably the only class of 'mitotic poisons' of potential value in the chemotherapy of malignant disease.

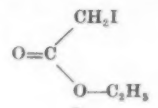
The last group comprises those compounds capable of destroying or preventing the formation of the mitotic spindle without any undue toxic effect upon the cell. Colchicine shows a far higher degree of specificity in this respect than any other substance known, although a very large number of chemically unrelated compounds have been reported as showing some degree of activity. The difficulty of correlating these chemically has led some authors to conclude that their properties are the consequence of physical rather than chemical attributes and that they may be likened in this respect to narcotics. It is difficult to believe, however, that colchicine is a 'structure non-specific' substance, and work reported herein may shed new light on this problem.

In addition to these three groups, there is a large number of other substances which have from time to time been reported as 'mitotic poisons'. No attempt is made to review or classify these chemically since, as we have already seen, the biological criteria upon which they have been judged are obscure and a critical appraisal is impossible. References are available in reviews by Lettré[21] and Astaldi *et al.*[3].

Class I: Non-Radiomimetic Mitotic Poisons

Dixon[22] has pointed out that lachrymators are of three types: (*a*) compounds possessing a positive halogen atom, that is, where the normal displacement of electrons in the carbon–halogen bond is reversed by an adjacent electron-attracting group such as the carbonyl group; (*b*) unsaturated compounds having an electron-attracting group adjacent to the double bond, thus permitting addition of nucleophilic reagents; (*c*) some arsenicals. Each type of compound will readily react with —SH groups, the arsenicals reversibly.

A series of 'mitotic poisons' may also be classified in this way, including the following: iodoacetic ester (I) and acid amide, maleic acid (II), unsaturated lactones such as parasorbic acid (III) and coumarin (IV), the quinones such as benzoquinone (V) with the quinonimines and diimines and arsenicals of the type of cacodylates and arsenoxides.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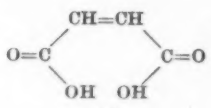
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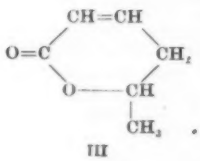
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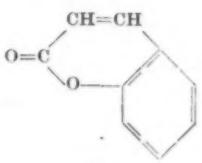
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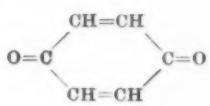

V

In Levan's[16] study of the cytological effects of a series of mono- and polyphenols, the greatest activity was found for those which were disubstituted in the *ortho* or *para* positions. It was left to Dustin[23] to direct attention to the fact that these are the ones which can oxidize to quinones, and there seems little doubt that this underlies their activity. Ostergren[16] has recently shown that coumarin and parasorbic acid have similar activity, but does not recognize the unsaturated character of both as the basis of activity. Haynes[24], in an excellent review of physiologically active unsaturated lactones, notes that —SH addition had been postulated as the mechanism of action, but points out that not all are antagonized by extrinsic thiols. Two possible explanations seem significant, namely, (1) the compound may react at two points, either the double bond and the carbonyl group (*cf.* reactions of unsaturated ketones[25]) or as an open-chain doubly unsaturated compound, or (2) reaction may occur with groups other than —SH, a faculty possessed by virtue of the electrophilic character of the double bond.

There seems little doubt that the activity of this group is in the main due to reaction with tissue —SH groups, and the high general toxicity and non-specific action is thus to be expected. The salts of heavy metals and organic mercurials as well as arsenicals likewise fall into the same category.

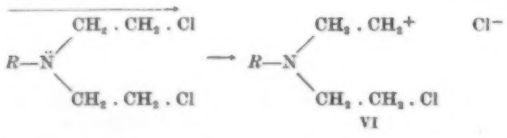
The reversibility of reaction of —SH groups with mapharside (3-amino-4-hydroxyphenyl arsenoxide) may explain the somewhat different cytological effects which it produces in comparison with compounds reacting irreversibly. Thus roots of *Vicia faba* treated with a sufficient dose to bring about complete arrest of mitosis show an apparently complete recovery. In experiments using *Triturus* larvæ

and already reported briefly[36], recovery was often accompanied by a stickiness of the chromosomes, producing terminal and intercalary bridges at anaphase. The latter occasionally produced fragments by rupture at the point of adhesion, an effect also noticed by Levan (*loc. cit.*) in *Allium* treated with phenols and by D'Amato[37] as the result of cold treatment. Barber and Callan[38] have also reported similar effects in *Triturus* as the result of cold treatment. It is highly important to distinguish between this effect and the type of breakage produced by radiation and vesicants which occurs in the *resting* nucleus.

Tests with hydroquinone performed in this laboratory on *Vicia* roots have not corroborated the results of Levan, and no evidence whatsoever of chromosome breakage was obtained.

Class II : Radiomimetic Compounds

The sulphur and nitrogen mustards owe their special reactivity to the electron-repelling character of the sulphur and nitrogen atoms which is derived from the lone pair(s) of electrons which they carry. As a consequence, ionization of the halogen is facilitated in aqueous solution, resulting in the production of a positive carbonium ion (VI) which is the initial reactant. In the case of the nitrogen mustards attention has recently been directed to this by Ross[39]. It may be depicted thus :



VI

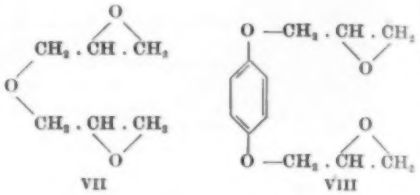
The behaviour of the second halogen will depend upon the manner of reaction of VI, but it is probable that it will follow the same course. The mustards are thus bifunctional alkylating agents, reacting readily with nucleophilic groups, notably ionized —SH, —COOH and phosphate groups, and also free —NH_2 by the S_N1 mechanism and suffering rapid hydrolysis in water. They thus stand contrasted with compounds of the iodoacetate type, where the group adjacent to the halogen atom is electron-attracting and reaction is by the S_N2 mechanism.

The requirement for 'radiomimetic' activity in compounds of this type appears to be the presence in the molecule of two alkylating groups having a minimum degree of activity[39]. In the case of the nitrogen mustards this has been measured by the rate of hydrolysis (Ross, *loc. cit.*). Since amino-groups are largely ionized and —SH un-ionized at physiological *p*H, it seems probable that the significant reaction is esterification of acid groups, possibly thereby bringing about cross-linkage between protein or nucleoprotein molecules[39]. Reaction with acid groups has been suggested by Mrs. Pirie[40] from a consideration of the binding of collagen by S-mustard and by Herriott *et al.*[41] working with a number of proteins. Furthermore, Elmore *et al.*[42] found that mustard gas reacted readily with the phosphoryl groups of nucleic acids, giving in the case of thymus nucleic acid one compound in which two groups were blocked per mol. of mustard.

Of great significance are the results of Herriott[43] on the inactivation of enzymes and viruses by S-mustard. He finds that viruses are more readily inactivated than enzymes and suggests this is due to reaction with nucleic acid. Further, those which contained deoxyribosenucleic acid were more susceptible than those having only ribosenucleic acid.

These results achieve a new significance in the light of Revell's[13] findings that the regions of breakage of *Vicia* chromosomes induced by N-mustards and di-epoxides are constant and bear a close relation to the distribution of heterochromatin ; that is, those regions which retain a 'nucleic acid charge' in the resting nucleus.

Following up the idea of cross-linkage of acid groups, Mr. J. L. Everett and Dr. W. C. J. Ross of this Institute have been preparing a series of di-epoxides, of which VII and VIII are typical :



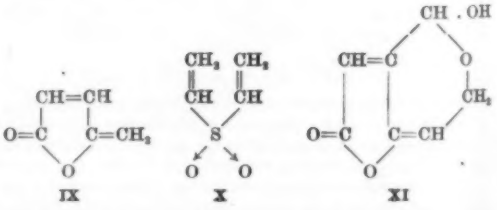
VII VIII

Di-epoxides were of particular interest among the various esterifying agents considered, since it was learned that compounds of this type are already in use in the textile industry for bringing about cross-linkage between carboxyl groups of wool fibres[44] (see footnote on p. 939).

These compounds show precisely the same cytological effects as the nitrogen mustards. Moreover, VIII is said to be vesicant[45], and there is evidence of its reacting by the S_N1 mechanism[46].

Unsubstituted NN-dichlorodiethylamine, which does not appear to have been tested previously, is also active, though less so than NN-di(2-chloroethyl)-methylamine.

Tests have also been made upon the other known vesicants, protoanemonin (IX) and divinyl sulphone (X). Attention was directed to these compounds since the double bonds might be expected to react strongly with nucleophilic reagents on the theory given earlier. In addition, however, they have two double bonds, that is, are bifunctional. Again, the cytological effects were similar to the mustards, though the compounds had an obviously high general toxicity, divinyl sulphone more so than protoanemonin. Patulin, which is non-vesicant and for which the structure (XI) has been proposed[47], has been found inactive. It must be considered as a member of Class I.



IX X XI

It seems a reasonable conclusion that all vesicants typified by slow healing of the primary lesion also

cause chromosome breakage, and that the latter is responsible for the healing difficulty. Also it might be held that the site and nature of the chemical reaction determining the cytological effect is the same in all cases, but that those which are less active, such as protoanemonin, are so because of the greater competition of the other reactive groups in the tissues, notably —SH. This is in agreement with the observed greater toxicity of the latter substance.

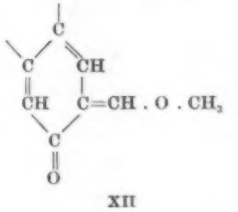
A number of substances of other types has been described as producing chromosome breakage similar to radiation, including aminostilbenes, carcinogenic hydrocarbons, urethane and caffeine. These observations, in the case of the first three, have largely been made on the Walker rat carcinoma[9] and it is impossible to say what was the ultimate mechanism. Certainly the evidence of tests upon *Vicia* and *Triturus* larvæ with urethane does not indicate any similarity of effect with the vesicants. Kihlman and Levan's[17] work with caffeine and other methyl xanthines has only so far been briefly reported. If, indeed, the effects prove to be similar, an entirely different mode of action, though one possibly associated with nucleic acid metabolism, must be sought. In addition, certain compounds have been described as mutagenic which do not fall into this class. A proper chemical appraisal of these findings is not at present possible.

Class III : Colchicine-type Compounds

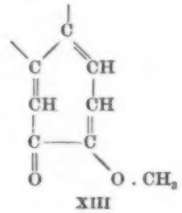
A great deal has been written concerning the action of colchicine and other compounds having like effects, and it is not intended to attempt any comprehensive review. As stated earlier, some authors, notably Ostergren[20], have concluded that nearly all organic substances show some degree of 'C-mitotic' action and suggest that spindle suppression is an aspect of narcosis.

It is rash to consider the relationship of structure to activity while that of colchicine is undecided; however, most authors agree that activity is lost if ring *C* becomes degraded. Thus, Steinegger and Levan[48,49] find '*iso*colchicine' and trimethyl colchicinic acid active, but loss of activity accompanies alteration of the *C* ring.

On Windaus's formulation[50] this ring has an *o*-quinonoid or quinone methide form (XII), while Dewar[51] has suggested, on theoretical grounds, a seven membered ring structure (XIII):



XII



XIII

More recently Cook and Somerville have succeeded in synthesizing 3 : 4 benztropolone[52] akin to XIII, but the biological properties do not appear to have been studied.

The methoxymethylene group of XII might be expected to be very reactive, and, indeed, the quinone-methides that have been described undergo rapid polymerization. If this be the structure, therefore, one could not regard colchicine as an 'inert' substance. XIII, on the other hand, could not be considered highly reactive.

In this connexion two results may be of significance: (1) Cornman[14] reports the occurrence of colchicine-type metaphases and the production of tetraploid cells in *Zea mays* after treatment with coumarin (IV). (2) In the experiments with protoanemonin (which possesses an exomethylene group as well as a second double bond) a very high incidence — up to 50 per cent—of spindle suppression was observed immediately after treatment, and a large number of tetraploid divisions after twenty-four hours. These observations on the effects of protoanemonin were not made in a previous study of its cytological effects[53] owing to the use of an experimental procedure unsuited to this type of investigation.

It appears that colchicine-like effects can be brought about by compounds which are both reasonably soluble and reactive. A series of compounds structurally analogous to components of the *C* ring according to both formulations are now being tested and details will be reported in due course.

The original work reported briefly above will also be published in full elsewhere.

III. Summary and Conclusions

Confusion in the use of the term 'radiomimetic' has led to erroneous judgments on the possible chemical basis of this action. Thus Dustin[33], taking 'pycnosis' as his criterion, has concluded that radiomimetic activity is characteristic of —SH-active compounds, whereas we believe that it is the non-specific 'toxic' effects which are predominantly characteristic of such substances. It is, moreover, suggested that the selective, truly radiomimetic action of such compounds as the mustards and other vesicants is due to their ability to react at sites *other* than —SH, probably by the esterification of acid groups. Possibly this work may also cast light on the problem of vesication.

It is, of course, well known that protein sulphur metabolism is of great importance in growth and cell division, and, clearly, substances blocking —SH groups have a profound effect upon the dividing cell. Whether the influence is exerted directly on the chromosome, through interference in the 2SH ⇌ S—S redox system or by enzyme immobilization, is not known.

The theoretical chemistry of the first two classes has been dealt with, largely bearing in mind the needs of the biologist who may not be aware of the principles involved.

If this analysis is accepted, the term 'mitotic poison' becomes invalid both biologically and chemically. The cell in division reveals the consequences of physiological derangement which remain undetected microscopically (though not biochemically) in the resting state. This is no justification for using the expression 'mitotic poison' in respect of unspecific toxic agents simply because their effect on the dividing cell has been described. The term might perhaps be applied correctly only to colchicine where there is an apparently selective action on an apparatus, the spindle, present only during cell division and essential to that process.

The main aim of work in this field must be to elucidate the possible mechanisms of mitotic inhibition and nuclear derangement, first, for the information they may give on the process itself, and secondly, for the discovery of useful growth-inhibitors.

As we have briefly indicated, compounds of the second class can serve both these functions and it may be in this direction that future research should be concentrated if useful progress is to be made in the chemotherapy of malignant disease.

We wish to express our gratitude to Prof. A. Haddow for interest and encouragement, and to Dr. W. C. J. Ross for much helpful discussion and advice, especially in connexion with the chemistry of the haloalkylamines and for valuable criticisms of the manuscript. Thanks are also due to Dr. D. A. Peak and the Boots Pure Drug Co. for the specimen of protoanemonin and their valuable co-operation in carrying out assays. The work upon which this paper is based has been supported by grants to the Chester Beatty Research Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the Research Grants Division of the U.S. Public Health Service.

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BIRD BEHAVIOUR

ON September 6, Section D (Zoology) of the British Association held at Newcastle upon Tyne a symposium on the subject of bird behaviour.

Mr. P. H. T. Hartley, speaking on "Routines in Bird Life", gave an account of some activities concerned in the maintenance of the individual bird. The value of such studies is three-fold: they are part of the basic ethology of birds; they provide the setting in which more complex actions must be studied and compared; and they throw light on certain ecological problems which are difficult of direct attack. In illustration of daily routines in feeding activity, herring gulls *Larus argentatus* in west Cornwall have three feeding periods in the day in the second half of September, separated by two resting periods; in the second half of October there are two feeds separated by a single rest. Blackbirds *Turdus merula* in Berkshire in winter feed all through the day, but are especially active in the hours after sunrise. The study of the feeding routines of two congeneric species, chiff-chaff *Phylloscopus collybita* and willow warbler *Ph. trochilus*, living in one wood showed that the chiff-chaffs forage consistently higher than willow warblers; this implies that the two species are not in close competition, although living on the same ground. The discovery of the same foods in two species does not necessarily imply competition between them. The different titmice of the genus *Parus* show ecological isolation, each species having its own feeding levels. The fact that any breakdown of species segregation is explicable by the occurrence of a temporarily superabundant food (such as caterpillars in early summer, and nuts or wild fruits in autumn) suggests that the possession of a separate feeding niche by each species at other times points to a genuine need to avoid interspecific competitions.

Mr. Hartley also gave examples of variations in routines of song utterance. In discussing the work of D. R. Barber on the song of the chaffinch *Fringilla cælebs* (see *Nature*, **161**, 277; 1948), he pointed out that any study of local variations in phrase length would be stultified if allowance were not made for the stage in the annual song cycle.

In his survey "Some Aspects of the Relationship between the Pair Bond and Breeding Economy of Birds", the Rev. E. A. Armstrong urged the need for an integrative approach to the study, in which psychological, ethological, morphological and physiological factors should be equally considered. He pointed out that at the time of the formation of the pair bond, there takes place a revolutionary change in the approach of each bird to another individual. Hostility or indifference must be replaced first by tolerance and later by co-operation, often with a fixed allotment of the roles in the breeding cycle.

When both sexes of a species are conspicuous, both share in the rearing of the young; and when there is colonial nesting the bright colours of the adults may function as a warning. In such colonial species as are conspicuous in coloration, it is almost inevitable that monogamy should be the rule of life, as there must be one parent always on duty at the nest. An unattended nest in a conspicuous colony offers an invitation to the raids of predators. In species wherein the male is conspicuous and the female cryptically coloured, the nest is hidden, and the hen usually bears the major part of the care of eggs or young. In such cases the species may be promiscuous or polygynous. In promiscuous species a 'lek' is used

for courtship assembly. In polygynous species the cock makes himself conspicuous by voice or appearance, and his territory is the rendezvous where he can be found by the hens. Mr. Armstrong said that he regards the provision of a rendezvous as a most important function of the territory in polygynous species. With bright colours which are aposematic in function, it is clearly necessary that both sexes should be so coloured; if only one sex were aposematically coloured, there would be selection as between the sexes.

Mr. Armstrong then developed the theory of social signals, or synepisematic coloration. He pointed out that in a number of species which often feed communally—avocets *Recurvirostra avosetta*, gannets *Sula bassana* and goldfinches *Carduelis carduelis*—the wings are conspicuously coloured, black and white, or black and gold. These brilliant colours may serve to signal to other members of the same species the existence of some temporarily or locally abundant food. Mr. Armstrong advanced the view that there is social selection as well as individual selection.

Environment may play a dominating part in the formation of the pair bond. In the snow bunting *Plectrophenax nivalis* the cock is conspicuous and the female cryptic; but the conditions of life are rigorous, the young are fed by both parents and the care of the newly fledged juveniles is rigidly divided between male and female. Should one parent die or desert, the young which are in its charge are allowed to starve by the other adult—so stringent has selection of behaviour been in the short northern summer. In the corn bunting *Emberiza calandra*, though the sexes are similar, there is frequent polygyny. Mr. Armstrong regards this as an adaptation to areas of especially abundant food. In support of this view he pointed out that the wren *Troglodytes t. troglodytes* is polygynous in England, but the St. Kilda wren *Troglodytes t. hirtensis* is monogamous. The Icelandic subspecies *Troglodytes t. islandicus* has polygynous tendencies. The appearance of the habit of polygyny in an area so far to the north of the range of a monogamous subspecies could possibly be attributed to the abundance of food in the Iceland birch scrub.

Dr. Robert Carrick began his talk, "The Feeding Reactions of Starlings", by a survey of Dr. David Lack's thesis that family size in birds is fixed by the fact that there is an increase in mortality as broods increase in size above a certain level, with the result that broods above the optimum in size produce fewer young per pair than broods of the optimum size. Lack and Arn have shown that in the alpine swift *Apus melba* the average number of young reared from clutches of four eggs is the same as the number reared from clutches of three. In the starling *Sturnus vulgaris* there is evidence of a greater growth-rate in broods of less than maximal size; but in the robin *Erithacus rubecula* the evidence is less satisfactory. In the study of Dr. Lack's theory, information is needed on four points: (1) that clutch size is inherited; (2) that there is under-nourishment in broods of more than optimal size; (3) that this under-nourishment is the principal cause of nestling mortality; (4) that the under-nourishment is the result of the inability of the parents to do better.

Dr. Carrick then gave an account of work on starlings bearing on the last three of these problems. Both sexes feed the young, the cock at one nest responding to auditory stimulation by bringing food while the chicks are yet cheeping within the egg. Several young are fed at each visit of the parent; up to the age of six days there is equality of distribution among the nestlings. An exception to this rule was found at a nest where six young were being reared by the female alone. Competition among the young increases when their eyes open. A hungry nestling has a great capacity to force its claim before the better fed members of the brood, and can make weight rapidly. The feeding-rate increases with the demand. By altering the numbers of birds in two broods, Dr. Carrick was able to show that there exists an immediate adjustment to brood size. This adjustment is made by an increase in effort on the part of the male. The larger the brood, the greater the contribution of the cock to the total feeding effort. A cock with a small brood reverts to pre-breeding behaviour and spends much time in song.

When the young are large, the stimuli to the parents are both visual and auditory. The parent will put food into the open gape of a dead nestling, despite the silence, and will take food to a covered cage in which a concealed nestling is calling hungrily. Each of the two releasers is therefore sufficient to guide feeding activity. There is a greater range of weight in broods of six than in broods of two or three: in the brood of six fed by a hen alone, the heaviest chick at the time of fledging was equal in weight to an average chick of other broods; the rest of the brood fledged under weight.

The discussion which followed centred largely on the feeding activities of parent birds. Prof. H. R. Hewer gave an account of the feeding activities of green woodpeckers *Picus viridis*; in this species both parents feed by regurgitation. The parents have a considerable storage capacity. Up to nine morsels may be produced in succession at one visit. The number of visits per hour is small—from one to something less than three. When the young grow large, two or three of the brood are fed at the nest entry, and the adult bird then pushes into the nest to feed the others. There is an integration of the feeding rhythms of male and female. At one nest a widowed female failed to rear the young, apparently as a result of loss of time wasted in indecision between the feeding and brooding drives.

Dr. C. Ellenby suggested that with so low a feeding frequency, there is time for all the nestlings to become hungry between the visits of the parents, including those most recently fed; there might, therefore, be an increased competition for any surplus food packets at each distribution. Mr. Armstrong pointed out that the capacity to store and to regurgitate food gives a greatly increased feeding-range. In green woodpeckers the scrabbling of the feet of the adult bird signals its coming with food. In wrens the parent sings a very soft song, and great tits *Parus major* have a short, soft note to attract the attention of sleeping or well-fed nestlings.

In reply to a question, Dr. Carrick said that he had attempted the experiment of establishing three broods of nine starlings; for various causes all these three experiments had been interrupted. Prof. G. C. Varley inquired if any data are available on changes in routine indicating times when availability of food is becoming a limiting factor. Mr. Hartley replied that in blackbirds there seems to be more feeding activity after noon on days of hard frost; but the winter routine of titmice suggests a slackening of feeding activity in the afternoon long before the onset of darkness prohibits the search for food. Mr. Armstrong said that, in contrast to this, wrens continue to hunt until late dusk.

OBITUARY

Sir Robert Pickard, F.R.S.

ROBERT HOWSON PICKARD was the eldest son of the late J. H. Pickard, of Edgbaston, Birmingham, and was educated at King Edward's Grammar School, Camp Hill; Mason College, where he studied chemistry under Tilden and P. F. Frankland; and the University of Munich, where he received his Ph.D. degree in 1898. A year later he was appointed head of the Chemical Department of Blackburn Technical College, and he became principal eight years later, at the early age of thirty-one. He held this dual post until he moved to London in 1919 to become principal of Battersea Polytechnic. Here he undertook additional duties as director of the newly formed British Leather Manufacturers' Research Association, an organisation with which he was later associated in an advisory capacity up to the time of his death. During this period he served on the Senate of the University of London and on the councils of the British Launderers' Research Association, the Boot, Shoe and Allied Trades Research Association, and on many important committees including the Burnham Committee, of which he was for some time secretary. He was director of the British Cotton Industry Research Association during 1927–43, vice-chancellor of the University of London (1937–39), chairman of the Chemical Council (1936–38), and president of the Institute of Chemistry (1936–39). He was a past president of the Society of Chemical Industry, twice vice-president of the Chemical Society, a member of the Research Committee of the Federation of British Industries, and chairman of the Committee of Directors of Research Associations. He was knighted in 1937.

This mere recital of the positions he held, remarkable though it may be, gives little indication of his most distinguished record. He infused life and vigour into everything with which he was associated. During the Blackburn period, his contact with the textile industry led him to see that there was wide scope for the application of science and scientific methods, and the extensive knowledge and experience thus gained proved to be of great use to him when he became director of the Shirley Institute. Another feature of the Blackburn period was his own research work. His main interest as a chemist lay in stereochemistry, and particularly in the relationship between chemical constitution and the magnitude of optical rotatory power. About 1905, in conjunction with his colleagues at Blackburn, he devised a method of resolving racemic secondary alcohols into their pure optically active isomerides. By this means, which proved to be of wide application, a number of homologous series of optically active alcohols and their esters were prepared and their rotatory powers for light of different wave-lengths determined. He was elected to fellowship of the Royal Society in 1917 while still at Blackburn, in itself a remarkable achievement and a great honour to a provincial technical school.

When the British Cotton Industry Research Association was formed in 1919, Pickard had hoped to be appointed director. Instead, he left Lancashire to take up the appointment at Battersea Polytechnic. Under his vigorous leadership the Polytechnic sprang to life in a way it never had before. I am told that his guidance at this time was literally the salvation of many ex-Service students seeking to repair the damages caused by years of mental stagnation. It is largely due to his insight and vision that the university side of the Polytechnic teaching activities was widened and encouraged. During this period he still continued his scientific work, but with decreasing intensity as the pressure of administrative duties bore increasingly upon him.

When the directorship of the Cotton Research Association became vacant through the death of Dr. Crossley, the position was advertised; but Pickard would not apply. Fortunately there were wise men in Lancashire who realized that he was the man for the post, and a deputation came to London and persuaded him to return to Lancashire. Thus he entered on what proved to be the greatest period of his career.

When he came to the Shirley Institute in 1927, he found that a vast amount of first-class scientific knowledge had been accumulated, but that after six years the industry was getting impatient and wanting more practical results. He saw that the time was opportune for an intensive application of the knowledge already gained, and for the introduction of special means to link the scientists more closely with the practical men in the mills. The success of his policy may be gauged from the fact that when he retired after seventeen strenuous years, the Research Association was recognized on all sides as an essential part of the textile industry and its name was known throughout the world. I would say he did more than any other man to justify the principle of the research association movement.

Pickard's other great interest was in education. He was for many years chairman of the Roedean School Council, member of the Courts of the Universities of Birmingham and Manchester, and in his later years a member of the Education Committee of the Surrey County Council. I have already referred to his connexions with the University of London. In 1948 he became chairman of Convocation, a position he held until shortly before his death. Many are the tributes that have been paid to the wisdom and sagacity he showed in those great and honourable positions.

He believed intensely in the value of leading the full life at school and college, and at his own College he was secretary of four societies and chairman of the Union. He was a great sportsman who excelled at cricket and tennis, and he associated himself closely with the social life of all the organisations he directed.

Pickard had a quick grasp of details and a remarkably retentive memory. He was a most severe critic, sometimes to the point of raising resentment in those he criticized. But he was also constructive, and the number is legion of those who have cause to thank him for advice and guidance in their life and work. He respected those who talked to him as frankly and fearlessly as he did to them. To some his outward bearing was somewhat harsh; but to know him intimately was to recognize a very human man with a high sense of moral values, whose word was his bond.

His family life was a happy one until a few years ago, when he suffered two severe blows, in the death of his wife and, shortly after, his only daughter. He is survived by an only son, at whose home in Surrey he died in his sleep on October 18, at the age of seventy-six.

Even the generous columns of *Nature* are not sufficient to do full justice to Pickard's life and work. In science and technology, industry and education, he has left the impress of a remarkable personality.

F. C. TOY

NEWS and VIEWS

Nobel Prize for Physiology and Medicine for 1949

THE Nobel Prize for Physiology and Medicine for 1949 has been awarded jointly to Prof. Walter Rudolf Hess, of Zurich, and Prof. Antonio Egas Moniz, of Lisbon.

Prof. W. R. Hess

PROF. HESS is professor of physiology in the University of Zurich. Thanks to his exceptional ability, Hess, originally a school teacher, obtained medical qualifications and adopted an academic career. His great energy and far-sightedness were responsible for the establishment of the High Altitude Research Station of the Jungfraujoch. This project met a long-felt need of scientific workers and was realized in 1931 with the help of an international foundation of which the Royal Society is a member. The earliest of Hess's physiological researches to attract widespread notice was his clear statement of the principles of autonomic nerve function. The medical world of the Continent owes to him the recognition of the 'ergotropic', power-increasing action of sympathetic nerve impulses, and the energy-saving or 'histotropic' action of parasympathetic stimulation promoting cell growth and repair. So early as 1925 he developed the technique which he has continued to use for investigating the function of individual regions of the brain. The method is to introduce needle electrodes into the brain of a cat and to stimulate very localized areas through these electrodes. The animals survive very well; special means are used for leading in the stimulating current, so that the animals can move freely. Motor effects of the stimulation are recorded cinematographically and analysed with the help of the film record. The brain tissue between the electrodes is then destroyed by electrocoagulation. The resulting disturbances, together with the effects of stimulation, allow conclusions to be drawn on the functions of the part of the brain concerned. The latter is identified with certainty by making histological preparations, plotted as an atlas of brain function. Last year Hess published a monograph which clearly outlines his conclusions on the relation of the diencephalon to motor activity. By these systematic and important researches, covering almost twenty-five years of tireless work, Prof. Hess has richly deserved the present award.

Prof. A. E. Moniz

PROF. MONIZ is a most distinguished neuro-surgeon whose international fame rests on two contributions to medical practice especially. Between 1927 and 1937 he introduced and developed cerebral angiography as a method of diagnosis of intracranial disease. All the essentials of the method at present in occasional use in neuro-surgical clinics are due to him. He published in 1936 a monograph on the operative treatment of certain psychoses, which described the operation of prefrontal leucotomy and the impressive results of its application to twenty cases of psychosis. Imagination, boldness and skill were necessary to demonstrate, as he did, the feasibility of the injection of radio-opaque substances into the internal carotid artery, and of the operative destruction of the white matter of the prefrontal lobes. He has described in his monograph how he came to devise leucotomy. He had noted how little the extensive removals of brain tissue by Brickner and Clovis Vincent had impaired social behaviour, and had considered the possibility of lesser removals of brain substance as a means of reversing the rigid functioning of groups of brain cells, which he thought to be responsible for the persistence in psychosis of painful ideas. The impetus to the first attempt came in London in August 1935, when he heard Jacobsen's description of his work with Fulton on the effects of frontal ablations on the so-called neurotic behaviour of chimpanzees. Assisted by Dr. Almeida Lima, he then perfected the technique of leucotomy within a few months

Although leucotomy is applicable in fewer cases and is more drastic than either insulin comas or electroplexy, the two other innovations which have recently revolutionized the treatment of mental disorders, the work of Prof. Moniz has exerted at least as important an influence, because he directed the attention of neuro-surgeons to psychiatric problems. The procedure which he devised may eventually be superseded; but the lesson which he has taught will not quickly be forgotten, for, with the neuro-surgeons who have followed him, he has played a large part in reviving in psychiatry a tradition of courageous and energetic treatment, and has demonstrated that skilful intervention may yield a degree of success even in the most serious and advanced cases of psychosis.

Botany at Trinity College, Dublin: Prof. H. H. Dixon, F.R.S.

PROF. H. H. DIXON, professor of botany in Trinity College, Dublin, retires at the end of this year. Prof. Dixon turned from a training as a scholar in classics at Trinity College, Dublin, to the field of plant physiology, which he studied with Strasburger in Bonn. He was then associated with the physicist, Dr. J. Joly, who became his intimate and life-long friend. Together they worked out and published the cohesion theory of the ascent of sap (1894): the mechanistic explanation of the transpiration stream which replaced older vitalistic theories. Dixon devoted the following decades to elaborating and establishing this theory by ingenious experiments in the wide field of physiology concerning the water-relations of plants. Apart from this, he did valuable work in connexion with the transport of metabolic materials and so forth. He became professor of botany in 1904, and from that time has made his laboratory the centre of active teaching and physiological research. He became a fellow of the Royal Society in 1908.

Dr. D. A. Webb

PROF. DIXON'S successor is Dr. D. A. Webb, a scholar of equally wide cultural interests. After graduation at Trinity College, Dublin, he went to Trinity College, Cambridge, where he obtained the degree of Ph.D. for a thesis on the "Distribution of Metals in the Tissues of Marine Animals". This biochemical and zoological research at the outset of his career gave place to experimental and field research in botany when he returned to Dublin as lecturer in Dixon's department. He published a students' Flora of Ireland, and initiated important research work upon the calcicole habit, upon the ecology of areas of western Ireland, and upon the critical taxonomy of certain groups of flowering plants such as the dactyloid saxifrages. He was joint organiser of the very successful International Phytogeographic Excursion to Eire this year,

and it is apparent that moderr field studies in Ireland will be profitably expanded under his guidance at Trinity College.

Sir Ambrose Fleming, F.R.S. (1849–1945)

NOVEMBER 29 marked the centenary of the birth of Sir Ambrose Fleming, who died as recently as 1945, at the age of ninety-five. Although Fleming is best known to the public for his invention in 1904 of the 'oscillation valve', the forerunner of the modern radio valve, he has other claims to be counted among the pioneers of radio. He was, in fact, the designer of the powerful transmitting station which, in December 1901, sent the first signals across the Atlantic, and, as scientific adviser to the Marconi Co. from 1899 onwards, he made many other important contributions during the early years of wireless communication. To commemorate the centenary of his birth, the Science Museum, South Kensington, London, is exhibiting, for two weeks from November 29, Fleming's original valve, and also on view is a collection of the original lamps and valves which he used in his early researches.

The Atlantic Cable and a Silver Thimble

A SILVER thimble of historic interest has recently been presented to the Science Museum, South Kensington, London, by Mr. R. B. Fitzgerald, nephew of the late Miss Emily Fitzgerald. The latter was the daughter of the Knight of Kerry upon whose land was built the telegraph house in which were terminated the first two Atlantic cables. After repeated failures in 1857 and 1858, the two cables from Valentia in Ireland to Newfoundland were successfully laid, and as an experiment they were connected together in Newfoundland so as to form from the Ireland end a continuous circuit some 3,700 miles in length. A cell was devised by borrowing Miss Fitzgerald's thimble, filling it with a few drops of acid and inserting a zinc wire. The current from this cell, which traversed the Atlantic and returned back again, was sufficiently strong to produce large deflexions on the reflecting galvanometer which had been recently devised by Prof. William Thomson, later Lord Kelvin.

New Satellites of Uranus and Neptune

IN British Astronomical Association Circular No. 312 some details are given regarding the two newly discovered satellites of Uranus and Neptune, respectively. Both were discovered by Gerard P. Kuiper during his search for new satellites with the 82-in. reflector of the McDonald Observatory, University of Texas. The new satellite of Uranus, now named Miranda, was discovered on February 16, 1948, magnitude 17, and is now known to have a period of about 33h. 56m. The motion is approximately circular and in the plane of the other four satellites. Neptune ii, for which the name Nereid has been proposed by the discoverer, was found on May 1, 1949, on plates exposed for forty minutes at the prime focus, with the mirror stopped down to sixty-six inches ($f/5$). Its magnitude was estimated to be 19·5, and later observations show that its period is about two years and that the plane of its orbit is within six degrees of the ecliptic. Kuiper says that, as Neptune could retain satellites nearly ten times as far away as Nereid, with periods up to about fifty years, further work is planned to cover the outer regions of the system.

Indian Dairy Research Institute: Silver Jubilee

THE difficulties of efficient dairying increase rapidly with the ambient temperature, and tropical dairying is beset with hazards which are not encountered in a more temperate climate. If children in hot countries are to be satisfactorily fed, and if, in countries such as India, the predominantly cereal diet of the great majority of the population is to be balanced by a sufficient intake of animal protein, fat, vitamins and lime, then tropical dairying, despite the difficulties, must be effectively practised. This is particularly important in India where religious sentiment is against the consumption of most types of animal food other than milk and dairy products.

What development there has been in dairying and dairy science in India during the past twenty-five years has been, in no small part, the result of the activities of the Indian Dairy Research Institute (formerly the Imperial Dairy Research Institute), which has just published a "Silver Jubilee Souvenir, 1923–1948" (pp. 45; Bangalore, 1948), with an interesting account of its development and progress since its establishment in 1923 at Bangalore. A very large proportion of the technical personnel—still grossly inadequate in numbers—of the Indian dairy industry, both the personnel engaged in improving the milk supply and those dealing with the technical aspects of milk distribution and manufacture, has been trained at this Institute, and most of the dairy research for the whole sub-continent is carried out there. Inadequate though its resources have been, and still are, to meet the enormous needs for development and technical improvement in every direction of Indian dairying, and despite past and present neglect by those in authority, the Institute has kept together a nucleus of well-trained workers and maintained a keen and hopeful spirit. With the solution of some of the most pressing political difficulties of the young Dominion, there can be little doubt that the Government, with the nutritional needs of the Indian people at heart, will support with adequate funds the well-considered scheme, already submitted to it, for the provision of more ample facilities for the future work of this Institute.

German Textile Industries during 1939–45

FOR some years before the Second World War, the German textile industries had been short of natural fibres such as cotton and wool. Substitutes therefore were sought in rayon and staple fibre, cottonized bast fibres (*Flockenbast*), paper and to a small extent in synthetics such as 'Perlon' and 'Pe Ce'. During the War, the difficulties were accentuated, and the chief aim of German textile technologists was to produce materials as similar to cotton or wool as possible and which would permit existing cotton or woollen machinery to be utilized. Rayon staple and, to a point, *Flockenbast* are genuinely useful fibres in their own right; but they were used by the Germans as substitute materials without regard to their inherent properties. The paper yarns were poor substitutes for the genuine article, though they found useful scope in the book cloth and artificial leather trades. These developments are described in a recent B.I.O.S. Overall Report (No. 13; pp. 178; London: H.M. Stationery Office, 1949; 3*s*.) which shows that the volume of fundamental research undertaken was small. There was, however, a high utilization-rate owing to the high level of technical ability among managers. Technical training at all levels was

fostered by excellent textile colleges, which were integrated with research institutes and official testing houses.

The Science Museum

THE presidential address of Dr. H. Shaw, director of the Science Museum, London, to the Museums Association has been published in the *Museums Journal* of August 1949, under the title of "The Science Museum and its Public". Dr. Shaw attempts an interesting analysis of the yearly million visitors to his Museum. He states that children form 25–30 per cent of the total, and affirms that the initiation of the Children's Gallery some twenty years ago where children are allowed to display natural exuberance is a complete success.

Institution of Civil Engineers: Awards

THE Institution of Civil Engineers has announced the following awards for papers read at meetings or published in the *Journal* during the session 1948–49. *The special thanks of the Institution* to Prof. J. F. Baker, for his paper on "A Review of Recent Investigations into the Behaviour of Steel Frames in the Plastic Range", he being ineligible, as a member of council, to receive an award. *Baker Gold Medal* to Major-General A. C. Fewtrell, in recognition of his work in connexion with the New Hawkesbury River Railway Bridge, New South Wales, Australia. *Telford Premium* to Dr. F. M. Lea and Dr. Norman Davey, jointly, for their paper No. 5722, "The Deterioration of Concrete in Structures". *Coopers Hill War Memorial Prize* to C. B. H. Colquhoun, for his paper on "The Brabazon Assembly Hall at Filton". *Telford Premiums* for papers read at meetings of the following Engineering Divisions: *Road Engineering Division*, R. M. Finch and R. R. W. Grigson, jointly; *Railway Engineering Division*, A. H. Cantrell; *Structural and Building Engineering Division*, P. O. Reece; *Works Construction Division*, H. J. B. Harding; *Maritime and Waterways Engineering Division*, J. A. Cashin; *Airport Engineering Division*, J. B. F. Hawkins. *Telford Premiums* for papers published in the *Journal* to: E. Leader-Williams and P. A. Badland, jointly; Dr. A. J. Ockleston; Prof. A. H. Jameson. *Miller Prizes* for papers by students of the Institution to: A. G. Preston, W. D. Coapes, J. Lindsay Smith, N. P. Roberts, P. B. Stewardson, K. A. Everard, E. W. Bennett, T. K. Chaplin. *Bayliss Prizes*, awarded on the results of the October 1948 and April 1949 examinations, respectively, to: K. S. L. de Fonseka and jointly to S. M. Joglekar and F. C. Speldewinde.

University of London

THE following appointments in the University of London have been announced: Dr. S. Devons, to a recently instituted University chair of physics tenable at the Imperial College of Science and Technology, from January 1, 1950; and Dr. E. W. Walls, to the S.A. Courtauld chair of anatomy tenable at the Middlesex Hospital Medical School, from October 1, 1949. The title of reader in anatomy in the University has been conferred on Miss R. E. M. Bowden, in respect of the post held by her at the Royal Free Hospital School of Medicine.

The following doctorates have been conferred: D.Sc., Prof. K. J. Franklin, University professor at St. Bartholomew's Hospital Medical College; Dr. Vera Fretter (Birkbeck College); P. H. Gregory (Imperial College); D.Sc.(Eng.), H. D. Conway (Queen Mary College and Battersea Polytechnic).

Conference of the Universities of Great Britain and Northern Ireland

THE 1949 Conference of the Universities of Great Britain and Northern Ireland, which has been convened by the Committee of Vice-Chancellors and Principals, will be held in the Beveridge Hall, University of London Senate House, during December 16–17. The programme consists of three sessions—one on December 16 and two on December 17—and the subjects and speakers will be, respectively: Sir Walter Moberly's book, "The Crisis in the University", Sir Walter Moberly and Prof. L. J. Russell; general education of students, Prof. F. T. H. Fletcher; place of technological education in university studies, Sir Lawrence Bragg, Sir Edward Appleton and Prof. Andrew Robertson. A printed programme, including the names of the university delegations and of specially invited guests, is in course of preparation. It is also hoped to include in this programme papers in connexion with the opening addresses. The printed programme will be distributed a few days before the Conference.

Announcements

DR. HERMAN MARK, director of the Polymer Research Institute at the Polytechnic Institute of Brooklyn, has been invited by the Indian National Research Council to visit India during January–February 1950 and to lecture on the scientific and practical aspects of the physics and chemistry of high polymers.

COLONEL L. C. HILL has been elected president of the Institution of Mining and Metallurgy for the session 1950–51 and will take office at the annual general meeting to be held on May 18. Colonel Hill was educated at St. Lawrence College and received his technical training at the Royal School of Mines, London. He graduated as B.Sc. (London) and A.R.S.M. (Mining) in 1912, being awarded the Brough Medal, and took up a post in Spain with the Rio Tinto Co., Ltd. The whole of his subsequent professional career has been with the same company.

THE Institution of Naval Architects is offering the following scholarships to British subjects, the closing date for entries being May 31, 1950, except for the Elgar scholarship for which the date is January 16, 1950. *For naval architecture:* the Elgar and Trewent scholarships, £175 a year, for shipyard pupils and apprentices. *For marine engineering:* the Parsons and Yarrow scholarships, £175 a year, for pupils and apprentices in marine-engine works; the Denny scholarship, £130 a year, tenable for four years at the University of Glasgow. Further particulars can be obtained from the Secretary of the Institution of Naval Architects, 10 Upper Belgrave Street, London, S.W.1.

THE Eighteenth International Physiological Congress will be held in Copenhagen during August 15–18, 1950. Preliminary programme and registration forms will be sent out at the end of this year and will, from January 1, 1950, be obtainable from local societies of physiology, biochemistry and pharmacology or from the Bureau of the Congress at Zoofysiologisk Laboratorium, 32 Juliane Mariesvej, Copenhagen Ø. The annual meeting of the Scandinavian Pharmacological Society will take place after the Congress, during August 19–20, and members of pharmacological societies outside Scandinavia will be invited to attend this meeting.

SOME METABOLIC EFFECTS OF ANDROGENIC SUBSTANCES

By Dr. D. PRICE, Dr. T. MANN and Dr. C. LUTWAK-MANN

Department of Zoology, University of Chicago;
Molteno Institute and Biochemical Laboratory, University of Cambridge

It was previously shown that the secretion of both fructose and citric acid in the male accessory organs of reproduction is governed by, and responds readily to, the fluctuations in the level of the male sex hormone. This close relationship made it practical to use the estimation of fructose and citric acid, either in semen or in the accessory glands, as a 'chemical indicator test' for the male hormone[1,2,3]. Recently, in the course of a metabolic study of transplants from accessory glands of the rat, it was found that when small pieces of male glands were dissected from young rats and transplanted subcutaneously into male or female hosts, such transplants grew readily in response to testosterone propionate or normally secreted testis hormone, and when fully developed exhibited a high content of fructose and citric acid[4,5].

To determine whether the secretion of fructose and citric acid in accessory reproductive organs can be stimulated also by other androgens, we have now carried out further studies upon the metabolic processes in (1) female prostate glands in normal females and in those treated with testosterone propionate, (2) male accessory glands in castrated males treated with synthetic progesterone, and (3) male accessory gland transplants in female hosts treated with gonadotrophin.

Secretion of citric acid in the female prostate gland. A prostate gland develops spontaneously in some female rats, and the incidence varies in different strains. Histologically this organ resembles the ventral prostate gland of the male rat; it can be stimulated by normally secreted androgens from the testis, the ovary and the adrenal cortex and by synthetic male hormone[6,7]. To determine whether the analogy between the female prostate and the male ventral prostate also extends to metabolic properties, the female gland was analysed for its content of citric acid, which is a characteristic secretory constituent of the male ventral prostate[8].

The experimental material was collected from an inbred stock of rats maintained at the Department of Zoology, University of Chicago, which has an 80 per cent incidence of female prostate. It was found that in a 42-mgm. sample of female prostate representing an aggregate from eleven normal two-month-old rats, there was 46 mgm. per cent of citric acid, or 2 μgm. per organ. In response to stimulation with testosterone propionate, there was a remarkable increase in the level of citric acid as well as an increase in the gross size and a change in the histological appearance of the female prostate (compare Figs. 1 and 2). From eleven female rats injected for three weeks with 200 μgm. testosterone propionate daily and autopsied at 85 days of age, 1,236 mgm. prostate tissue was recovered; this contained 1,380 μgm. citric acid, which corresponds to 112 mgm. per cent or 125 μgm.

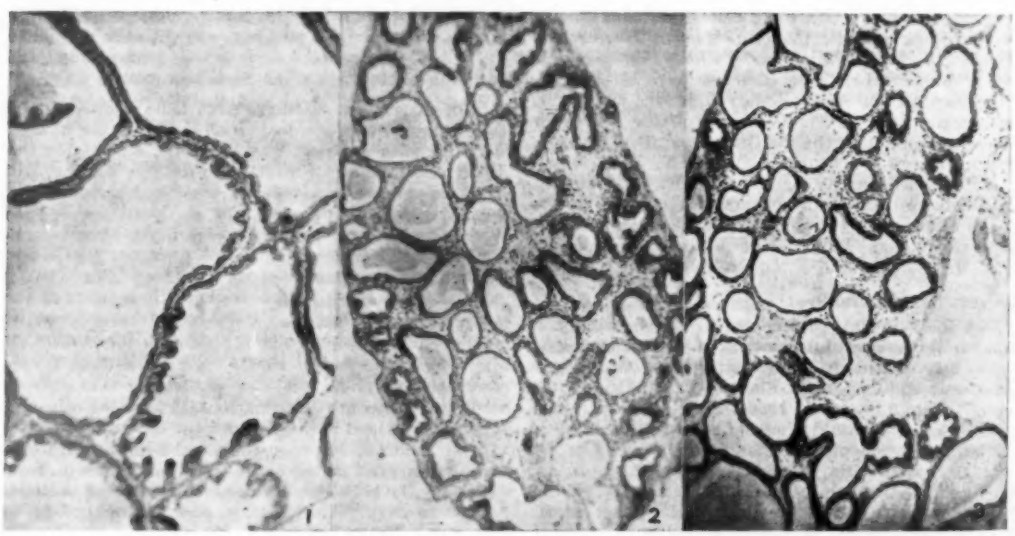

Fig. 1. Prostate gland of a female rat 85 days old injected with testosterone propionate for three weeks prior to autopsy. Note the distended acini and the tall columnar epithelium. × 56

Fig. 2. Prostate gland of a normal untreated female rat 85 days old. × 56

Fig. 3. Prostate gland of a normal untreated female of approximately sixty days of age showing the histological condition of the gland at the age at which testosterone propionate injections were begun. × 56

per organ. Another group of thirteen females received the same dose of hormone for two weeks; here the total tissue collected was 1,012 mgm., containing 1,427 μgm. citric acid, a concentration of 141 mgm. per cent or 110 μgm. per organ. For comparison, determinations were also made on the ventral prostate of male rats; thus in the ventral prostate of males 36–40 days old, there was 44 mgm. per cent or 29 μgm. per organ, in rats 85 days old 39 mgm. per cent or 121 μgm. per organ of citric acid.

These findings bear out the close metabolic resemblance between the male ventral prostate gland and the female prostate, and they show that the prostate of normal untreated females secretes citric acid.

Secretion of citric acid and fructose in male accessory glands in response to progesterone treatment. This series of experiments was carried out to ascertain whether administration of the corpus luteum hormone, progesterone, produces androgenic effects that are biochemically detectable. Effects of progesterone upon the weights and histology of the male accessory glands have been reported (see ref. 9 for recent literature). Twenty-one male rats were castrated at the age of eight to ten weeks, left for nine weeks, and then divided into three groups: (I) untreated; (II) 25 mgm. progesterone ('Proluton' Schering) injected daily for three weeks; (III) 5 μgm. testosterone propionate injected daily for three weeks; in addition there was group (IV) normal non-castrated rats of the same age as groups I, II and III. All animals were 20–22 weeks old at autopsy. Their accessory glands were analysed for citric acid and fructose, as well as for total nucleic acid phosphorus. In this experiment, unlike in our previous studies, the dorsolateral prostate was subdivided by careful dissection into its dorsal and lateral components, each of which was separately analysed. Results are summarized in Table 1.

Table 1. Behaviour of male accessory glands in response to progesterone

Organ	Group of rats*	Weight (mgm.)	Citric acid μgm./ organ	Citric acid mgm. %	Fructose μgm./ organ	Fructose mgm. %	Nucleic phosphorus μgm./ organ	Nucleic phosphorus mgm. %
Ventral prostate	I	14	1	8	0	0	19	133
	II	23	10	45	0	0	26	112
	III	16	4	28	0	0	16	97
	IV	339	232	69	0	0	246	73
Coagulating gland	I	7	0	0	0·3	4	14	197
	II	13	0	0	7	55	17	132
	III	8	0	0	1·4	18	12	152
	IV	132	0	0	348	263	84	64
Seminal vesicles	I	27	0·6	2	0	0	30	112
	II	40	5	12	0	0	39	98
	III	30	1·4	5	0	0	28	94
	IV	962	695	72	0	0	400	41
Lateral prostate	I	7	0·3	4	0·3	4	12	185
	II	29	0·4	1·6	8	28	26	89
	III	12	0·2	3	0·8	7	12	102
	IV	168	63	37	220	131	108	64
Dorsal prostate	I	9	0	0	0·3	4	11	124
	II	16	0	0	2	12	10	64
	III	9	0	0	0·3	3	9	104
	IV	75	0	0	56	75	38	51

* Experimental animals: Group I, castrated, untreated; Group II, castrated, treated with progesterone; Group III, castrated, treated with testosterone propionate; Group IV, non-castrated controls.

Treatment of the young male castrates with relatively large doses of progesterone brought about a distinct stimulation of metabolic activity in all accessory glands, and judging from the values for citric acid and fructose, it even exceeded that due to very small doses of testosterone propionate. The weight of the organs, on the other hand, and the nucleic acid phosphorus content, which presumably expresses the cellularity of these organs, were increased by progesterone in a less conspicuous manner than the secretion of fructose and citric acid. In connexion with nucleic acid phosphorus, it is interesting to note that whereas the absolute content of it in the accessory glands (μgm. per organ) was highest in normal non-castrated rats, its concentration (mgm. per cent) was lowest in this group, because of the considerable accumulation in these glands of secretory fluid which is itself devoid of nucleic acid.

It is clear from the results summarized in Table 1 that large doses of progesterone ('Proluton') were capable of producing androgenic effects in all accessory organs of male castrates.

Secretion of citric acid and fructose in transplants of male accessory glands in female hosts treated with gonadotrophin. In earlier studies it was shown that gonadotrophic treatment of female rats increased the production of ovarian androgens as judged by increase in weight and stimulation in the histological condition of the female prostate gland; in spayed females injected with gonadotrophin, no stimulation of the female prostate was found[7]. In addition, male ventral prostate transplants were strongly stimulated in pregnant and lactating female hosts, as were also the female prostate glands in some of the hosts[10]. To determine whether transplants of male accessory glands secreted fructose and citric acid in response to androgenic stimulation in female hosts, the following experiment was performed. Twenty female rats aged 27–70 days served as hosts; transplants were made of the coagulating gland, the ventral, lateral and dorsal prostate, from thirty-three male donors aged 27–70 days. Immediately following implantation, the female hosts were injected daily with 20 international units of equine gonadotrophin ('Gonadin', Cutter Laboratories) for 30–32 days.

It was found at autopsy that treatment with 'Gonadin' had a striking effect on the growth of the transplants and on the reproductive organs of the females. The behaviour of the transplants in regard to their metabolic activity is shown in Table 2.

Table 2. Transplants of male accessory glands in female hosts treated with gonadotrophic hormone

Transplant	Citric acid (mgm. %)	Fructose (mgm. %)	Nucleic phosphorus (mgm. %)
Ventral prostate	34	0	27
Coagulating gland	0	28	54
Lateral prostate	15	12	52
Dorsal prostate	4	17	53

The results demonstrate clearly that metabolically active transplants of male accessory organs were maintained in female hosts. The indications are that this metabolic effect is due to ovarian androgens.

A detailed histological examination of tissues was carried out in experiments 1, 2 and 3, and details will be published in due course.

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NEW ALKALI METAL PERBORATES

By Dr. A. H. FATHALLAH
AND
Prof. J. R. PARTINGTON, M.B.E.
Chemistry Department, Queen Mary College, University of London

THE alkali perborates have been regarded by some as addition compounds of hydrogen peroxide and metaborates[1], and by others as true persalts not containing hydrogen peroxide as such[2]. Le Blanc and Zellmann[3] divided them into (*a*) true perborates MBO_3; (*b*) pseudo-perborates $M(BO_2H_2O_2)$ with firmly bound hydrogen peroxide (*M* is a univalent metal and (*a*) and (*b*) have one atom of active oxygen per atom of boron); and (*c*) addition compounds with loosely bound hydrogen peroxide, for example, $Na(BO_2H_2O_2).2H_2O_2$. This differentiation into pseudo- and true perborates was not confirmed by Menzel and co-workers[2]. Among the perborates so far investigated, there is insufficient evidence for the existence of compounds in which the amount of water present does not permit the total active oxygen (O_a) to be present as hydrogen peroxide.

The following alkali perborates (derived from metaborates) are reported in the literature. (1) $Li_2B_2O_3.2\frac{1}{2}H_2O$ ($O_a : B = 0{\cdot}5 : 1$) prepared by Bezner-Lowy[4]; on account of its low active oxygen content, it was not regarded by Menzel as a chemical individual. (2) $LiBO_3.2H_2O$ or $LiBO_2H_2O_2.H_2O$ ($O_a : B = 1 : 1$), prepared by Menzel. On dehydration it forms $LiBO_3.H_2O$ (or $LiBO_2.H_2O_2$) without loss of active oxygen, but further dehydration results in loss of active oxygen and the formation of a labile product forming gaseous oxygen and not hydrogen peroxide with water or acids. (3) $NaBO_3.4H_2O$ or $NaBO_2H_2O_2.3H_2O$ ($O_a : B = 1 : 1$), isolated by Melikoff and Pissarjewsky[5] and Tanatar[6], and described in numerous patents. On dehydration, this gives $NaBO_3.H_2O$ (or $NaBO_2H_2O_2$) and otherwise behaves in the same way as (2). (4) $NaBO_3$ ($O_a : B = 1 : 1$), a formula given from the active oxygen content alone by Le Blanc and Zellmann[3] to a product formed from boric acid and sodium hydroperoxide; its existence was not confirmed by Menzel. (5) $Na(BO_2H_2O_2)$, $2H_2O_2$ or $NaBO_3.3H_2O_2$ ($O_a : B = 3 : 1$), the first formula being given by Le Blanc and Zellmann[3]; the formation of a sodium perborate with high active oxygen content had already been claimed in some German patents[7]. (6) $2KBO_3.H_2O$ or $KBO_3.\frac{1}{2}H_2O$ ($O_a : B = 1 : 1$), isolated by Girsewald and Wolokitin[8]. (7) $2KBO_3.H_2O_2$ or $KBO_3.\frac{1}{2}H_2O_2$ ($O_a : B = 1\frac{1}{2} : 1$), also obtained by Girsewald and Wolokitin. (8) $KBO_3.H_2O$ ($O_a : B = 2 : 1$), isolated by Bosshard and Zwicky[2], who did not regard (7) as a chemical individual. (9) $RbBO_3.H_2O$ ($O_a : B = 1 : 1$), and (10) $CsBO_3.H_2O$ ($O_a : B = 1 : 1$), obtained by Christensen[9].

In the lithium, rubidium and cæsium perborates so far isolated, the active oxygen never exceeded one atom per atom of boron, whereas in sodium and potassium perborates the active oxygen reached three and two atoms per atom of boron, respectively. It is also seen that only in (6), (7) and (8) is the amount of water less than that which is necessary if the total active oxygen is present as hydrogen peroxide. Krauss and Oettner[1], however, regarded the small percentage of water in $KBO_3.\frac{1}{2}H_2O$ as due to experimental error, and they do not refer at all to $KBO_3.H_2O$.

In our investigations of the alkali perborates, the existence of $KBO_3.\frac{1}{2}H_2O$ and $KBO_3.H_2O$ has been confirmed. Re-investigation of the German patent 256920 has shown that the active oxygen in sodium perborate can reach two atoms per atom of boron when $NaBO_3.4H_2O$ is treated with sufficient 30 per cent hydrogen peroxide and the solution precipitated with alcohol, or the sparingly soluble perborate is allowed to crystallize by cooling. Crystallization of the perborate does not take place when excess of hydrogen peroxide is present, but after evaporating the solution under reduced pressure over phosphorus pentoxide at room temperature, and washing the viscous mass formed with alcohol and ether, a crystalline solid was obtained in which the active oxygen reached three atoms per atom of boron. In both cases, dehydration in vacuum at room temperature over phosphorus pentoxide resulted in the formation of products which, from the percentage of water and active oxygen they contain, seem to be undoubtedly true persalts.

The amount of active oxygen could be increased in lithium, potassium, rubidium and cæsium perborates beyond the values given in the literature, and the following new compounds were obtained: (1) $LiBO_3.H_2O$ ($O_a : B = 2 : 1$), obtained by evaporating a solution of lithium metaborate ($LiBO_2.8H_2O$) in 30 per cent hydrogen peroxide ($LiBO_2 : H_2O_2 = 1 : 3$) under reduced pressure (about 5 mm. mercury) over phosphorus pentoxide at room temperature, and washing the viscous mass obtained with alcohol and ether, when a white crystalline solid was formed. This was converted into a product having the above formula by further drying in vacuum over phosphorus pentoxide at room temperature, or by heating in vacuum at 45° C. By dissolving this perborate in excess of 30 per cent hydrogen peroxide and evaporating in the same way, no increase in active oxygen was observed.

(2) $KBO_3.H_2O$ ($O_a : B = 3 : 1$), obtained by treating Bosshard and Zwicky's potassium perborate with excess of 30 per cent hydrogen peroxide and evaporating to dryness under reduced pressure as above. After washing the white solid obtained with alcohol and ether it corresponds with the above formula.

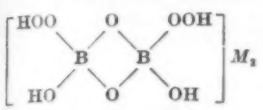
(3) $RbBO_3.\frac{1}{2}H_2O$ ($O_a : B = 2 : 1$), obtained by adding 30 per cent hydrogen peroxide ($RbBO_2 : H_2O_2 = 1 : 3$) to a concentrated aqueous solution of rubidium metaborate (obtained by fusing equivalent amounts of boric acid and rubidium carbonate) and allowing the perborate to separate out by cooling. The white crystalline precipitate formed was washed with alcohol and ether and dried over phosphorus pentoxide in vacuum at room temperature or by heating in vacuum at 45° C., when the product corresponded with the above formula. By precipitation from the mother-liquor with alcohol the same perborate is formed. By treating this perborate with excess of 30 per cent hydrogen peroxide and evaporating as above, the active oxygen content increased, but did not reach three atoms per atom of boron.

(4) $CsBO_3.\frac{1}{2}H_2O$ ($O_a : B = 2 : 1$), prepared in the same way as the corresponding rubidium salt. By treatment with excess of 30 per cent hydrogen peroxide the active oxygen increased; but, as in the case of the rubidium salt, it did not reach three atoms.

It seems, therefore, that all the alkali perborates containing more than one atom of active oxygen per atom of boron (in contrast to lower perborates) always form true persalts on dehydration. Perborates with more active oxygen than two atoms per atom of boron are unstable, the instability increasing with rise of atomic weight of the alkali metal. This

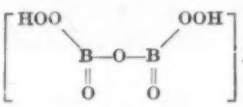
accounts for the fact that cæsium and rubidium perborates with three atoms of active oxygen, analogous to the sodium and potassium salts, could not be isolated in a pure state. Lithium is exceptional, since no lithium perborate with an active oxygen content higher than two atoms per atom of boron could be detected. The differentiation into pseudo- and true perborates could not be confirmed.

By analogy with Menzel's dimeric formulæ for lower perborates represented by I and II, the dimeric formulæ III and IV are suggested for perborates containing two atoms of active oxygen per atom of boron. No free hydrogen peroxide is present and the formulæ explain the behaviour of these perborates on dehydration.



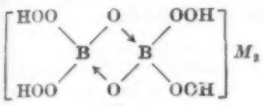
I

M = Na or Li



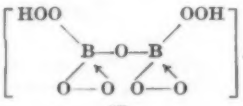
II

M = K or NH_4



III

M = Na or Li



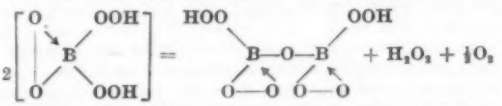
IV

M = Rb or Cs

In the formulæ the valencies attached to each boron atom are formulated as follows. Three of them originate from the normal three valencies of the boron atom and the fourth by a co-ordinate link directed from the oxygen to the boron atom. Hermans[10] regarded all the four links as equivalent.

In III there are two atoms of active oxygen and one molecule of constitutional water per atom of boron; this formula may represent sodium and lithium perborates, since it explains their tendency to retain one molecule of water per atom of boron, and their different behaviour from the lower perborates.

In IV there are two atoms of active oxygen and 0·5 molecule of constitutional water per atom of boron, and this formula may represent rubidium and cæsium perborates. Bosshard and Zwicky's potassium perborate, which tends to retain less than one and more than 0·5 molecule of water on dehydration, may contain anions represented by both formulæ. Higher perborates containing more than two atoms of active oxygen, for example, KBO_3,H_2O, may be derived from an ion represented below, and their instability on dehydration may be explained if it is assumed that this anion has a tendency to associate to form anions containing less active oxygen.



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THE NATIVE FORESTS OF CUYAHOGA COUNTY, OHIO

In a recent publication*, Dr. Arthur B. Williams discusses a study undertaken into the character and composition of the forest cover of Cuyahoga County, Ohio, as it existed at the time when the first band of white men under Moses Cleveland appeared on the banks of the Cuyahoga River in 1796. The native forest had at that time been little modified by human agency, even by Indian influence, since for many years this part of Ohio had been regarded as a sort of 'no-man's-land' between Indian and white. The 152 years which have since elapsed have witnessed the disappearance of the forest. Since many of the species of this forest community are known to have exceeded three hundred years in age, the author states "it is evident that some of the remnants of the forest of Moses Cleveland's day may still be in existence, as in fact they are. Many of these old landmarks have disappeared and the number of survivors of the forest of 1796 is becoming rapidly less and the task of reconstructing the picture of the original forests becomes increasingly difficult."

It is said that the natural vegetation of the entire State has been studied and outlined in a general way. The value of such studies, as is well understood, is that they contribute to our understanding of the environment in which the civilization of the present day had its origins and in which, though now greatly modified, we, in these days, live. In our day, and this applies to many parts of the world, the author says that it is almost impossible for the average city dweller (and he might have added country dweller) to visualize the density and character of the forest which once covered the land of the County. This is not only because very few remnants of original vegetation now remain, but also because very few such remnants are to be found anywhere else in the eastern part of the United States. It has been frequently emphasized that no other part of North America has been so profoundly altered by the works of man as has this section of the Continent.

As was inevitable, the removal of the forest with its dense protective canopy has produced a profound change in the climate now experienced by the mass of cities and villages which covers the County at the present time. In other countries of the world, now often occupied by deserts or characterized by semi-desert conditions, the destruction of the forest and the resultant climatic changes have been brought about by a small population over long periods of time covering hundreds or thousands of years. This renders the present study, while of high ecological importance, the more striking. In India half a century ago and more, from rough studies made by forest officers, the remnants of previous great forests then represented by individual, or clumps of, old trees scattered over agricultural or grazing lands were noted and recorded in different parts of the country for a varying type of species. There were no opportunities or leisure for research work in those days, and nothing like the detailed and informative study carried out by Dr. Williams, for which he and the Holden Arboretum may be congratulated, was possible.

* The Native Forests of Cuyahoga County, Ohio. By Dr. Arthur B. Williams. Scientific Publications of the Cleveland Museum of Natural History, Vol. 9 (Holden Arboretum Bulletin No. 1). Pp. 90. (Cleveland, Ohio: Cleveland Museum of Natural History, 1949.)

LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications

Inhibiting Action of some Analogues of Folic Acid on the Growth of Plant Tumours

ANALOGUES of folic acid have been found capable of inhibiting the growth of the Rous sarcoma in chickens[1] and sarcoma 180 in mice[2], of causing a remission in leukæmic children[3] and of prolonging the survival of leukæmic mice[4]. The effect of twelve of these analogues (all samples of folic acid and its analogues were kindly supplied by Lederle Laboratories, Pearl River, New York) on the growth of tumours induced by the crown gall bacterium on carrot tissue has been tested. Cylinders of tissue 10 mm. diameter × 6 mm. high were removed as described in a previous communication[5], and inoculated with virulent crown gall bacteria. Four days later, when the first signs of tumour formation became visible along the line of the cambium, 0·05 ml. of a 1/1,000 solution of the folic acid analogue to be tested was dropped on to, and spread over, the surface of the tissue. The amount of substance applied was 0·05 mgm. per fragment. Sterile distilled water was applied to the control group. Twenty carrot fragments were used in each test. The accompanying table shows the percentage of fragments which had developed macroscopically visible tumours four weeks after treatment had been applied.

Percentage of carrot fragments with macroscopically visible tumours 4 weeks after treatment with 0·05 mgm. of folic acid analogues

Compound	% Tumours	Compound	% Tumours
4-amino-PGA	0	N^{10}-methylpteroic acid	90
4-amino-N^{10}-methyl-PGA	0	9-methyl-PGA	100
4-amino-9, N^{10}-di-methyl-PGA	0	4-aminopteroyl aspartic acid	90
4-amino-9-methyl-PGA	0	4-aminopteroyl-*dl*-2-alanine	100
4-aminopteroyl-γ-glutamyl-γ-glut-amyl glutamic acid	0	4-aminopteroyl-*dl*-threonine	90
Pteroylaspartic acid	100	Pteroylglutamic acid (folic acid)	100
Pteroyl-*dl*-aspartic acid	100	Control	100

Five compounds, issued by Lederle Laboratories under the names 'Aminopterin', 'A-methopterin', 'A-denopterin', 'A-ninopterin' and 'Amino-teropterin', were thus found capable of suppressing completely the growth of tumour tissue induced on carrot by inoculation with crown gall bacteria, at a dosage level of 0·05 mgm. per fragment. The tumour tissue which had begun to form frequently turned brown and was probably killed. A dose of 0·0005 mgm. of these substances very greatly reduced tumour growth. At this low dosage-level the inhibition could be partially reversed by the addition to the solution of 10 mgm. per ml. of folic acid. Details of these reversal effects and a description of the comparative action of these compounds on tumour and non-tumour tissue will be published elsewhere.

It is of interest that all five compounds which proved capable of inhibiting growth of crown gall tumour tissue have also been shown to inhibit the growth of several animal tumours[6]. This finding suggests a fundamental similarity between the folic acid metabolism of the plant and animal cell. It also suggests that carrot fragments on which tumours have been induced by crown gall bacteria may provide convenient test objects for the screening of compounds for their tumour-inhibiting action.

This work was done in part under an American Cancer Society grant recommended by the National Research Council Committee on Growth.

R. S. DE ROPP

New York Botanical Garden,
New York 58, N.Y.

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Hæmogram, Serum Protein and Plasma Volume of Healthy, Well-nourished East Africans in Uganda

IN the course of an investigation on anæmia in Kampala, Uganda[1], it was found necessary to establish standard hæmatological and other values to enable the investigator to assess the degree of recovery. It was found that these values were the same as had been found in Europeans[2,3,4], North Americans[5] and Indians[6], the only exception being the albumin/globulin ratio.

The subjects were fit male adults belonging to the African upper class. They were county and district chiefs, ministers and other high officials in the Buganda Native Government, students and nursing orderlies. These men, thirty-four in all, could afford to eat as much food as they wanted, though, with the exception of the students, they were living mainly on a vegetarian diet. The thirteen students who consumed meat and milk regularly were compared with fourteen of the other subjects, of whom it was made reasonably certain that they were near-vegetarians. There was no significant difference between the two groups in the hæmogram and in the value for total serum protein. But in the students, serum albumin was significantly higher (P.E.D. $< 0{\cdot}0001$) and the globulin correspondingly lower (P.E.D. $< 0{\cdot}04$). In the whole group of thirty-four subjects, there was a negative association between albumin and globulin levels, the coefficient of correlation being $-0{\cdot}7$.

All subjects wore shoes regularly and were thus protected against massive hookworm infestation. Of twenty-two who permitted their stools to be tested, eleven showed no hookworm ova, although several samples were investigated and the concentration method was used. The eleven hookworm carriers did not differ from the eleven non-hookworm carriers in their hæmatological and serum protein values. Six hookworm carriers agreed to be purged, and the hookworms removed never exceeded fifty. There was no alteration in the hæmogram following the 'worming'. Eight of the thirty-four volunteers were carriers of the sickle cell trait; they did not differ from the rest in their hæmogram. This was to be expected, as in a mass survey[7] in Uganda no correlation had been found between anæmia and sicklæmia. The incidence of the sickle cell trait in a given population depends on its tribal composition rather than on its state of health[8].

Table 1. Hæmogram and serum protein in 34 healthy, well-nourished East Africans

	Hæmoglobin (gm. %)	Red cells ($\times 10^6$/c.mm.)	Packed cell volume (%)	M.C.V. (cubic μ)	M.C.H. ($\gamma\gamma$)	M.C.H.C. (%)	Serum protein (gm. %)	Serum albumin (gm. %)	Serum globulin (gm. %)
34 Males	16·5±1·02	5·5±0·4	48·1±2·7	87·3±3·8	30·0±1·9	34·3±1·7	7·17±0·44	4·97±0·53	2·20±0·56
13 Students	16·5	5·5	49·0	88·8	30·0	33·8	7·29	5·29	1·97
14 Non-students (near vegetarian)	16·4	5·5	47·6	86·2	29·8	34·6	6·99	4·49	2·50
11 Hookworm carriers	16·3	5·45	47·5	87·2	30·0	34·4	7·02	4·94	2·08
11 Non-hookworm carriers	16·2	5·4	47·8	88·9	30·2	33·9	7·20	5·00	2·20
8 Sicklæmics	16·4	5·6	48·9	87·3	29·3	33·5			
26 Non-sicklæmics	16·5	5·5	47·9	87·1	30·0	34·4			

Eleven subjects permitted the determination of their plasma volume. The total circulating values agreed with those found in healthy Caucasians and Indians.

Table 2. Total circulating plasma and blood values in 11 healthy and well-nourished East Africans

Blood volume (ml.)	Plasma volume (ml.)	P.V./cm. height (ml.)	P.V./10 cm.² surface (ml.)	P.V./kgm. weight (ml.)
4,850 ± 483	2,773 ± 89	16·65 ± 1·38	16·7 ± 1·3	47·2 ± 5·4

Hæmoglobin (gm.)	Serum protein (gm.)	Serum albumin (gm.)	Serum globulin (gm.)
775 ± 101	194 ± 22	131 ± 13	62 ± 22

The methods used were practically identical with those employed in a similar investigation on Indians[6]. The only differences were that hæmoglobin was determined by a modified cyan-hæmatin method[9], and that, calculating the blood volume from the hæmatocrit and the plasma volume determined by the Evans blue method, allowance was made for an 8 per cent plasma content of the packed cell column[4].

H. LEHMANN

Makerere College and Mulago Hospital,
Kampala, Uganda.
Oct. 15.

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Action of β-Amylase on Amylose

THE constituent of starch, usually called amylose, which consists of unbranched glucosidic chains, is hydrolysed by β-amylase in step-wise fashion, two glucosidic residues being detached at a time. There is growing evidence that the chains in a sample of amylose are of widely varying lengths—a sort of a homologous series.

Swanson[1] has concluded that the enzyme, having attacked one chain, completes its hydrolysis before attacking another. The evidence furnished consisted in readings of iodine coloration and of products of dialysis of the reaction mixture during β-amylolysis. The observations indicated the absence of short-chain products. Cleveland and Kerr[2] came to much the same conclusion. When a limited addition of enzyme was made to corn amylose and the reaction interrupted at certain stages, the unconverted residues appeared to have mean molecular weights comparable with that of the original amylose. Measurements of viscosity, reducing power and iodine coloration were used in arriving at this conclusion, and further, that the shorter chains of amylose are preferentially hydrolysed, from which Swanson's 'single-chain' hypothesis received support.

Hopkins, Jelinek and Harrison[3] also used the device of interrupting the hydrolysis, but had interpreted the increasing resistance to the β-enzyme exhibited by the successive amylose residues as indicating that the longer chains were more easily hydrolysed than the short ones. A further clue lies in the changes in iodine coloration. If β-amylase removes the short chains preferentially, leaving an increasing proportion of long ones in the residue, the latter would continue to give blue with iodine and the peak of the absorption curve would remain in the same position (wave-length) as that of the original amylose. Swanson's experiments indicated this. If, on the other hand, chains of all lengths are liable to simultaneous attack without preference, all being shortened at the same rate, a shift in the absorption curve peak would be expected to occur sooner or later, the iodine coloration becoming redder. The experiments of Hopkins *et al.* pointed this way.

To settle this question, we prepared an amylose fission product of mean chain-length about twenty glucose units by acid hydrolysis of potato amylose followed by the removal of any residue of long-chain material by *cyclo*hexanol and of very short-chain products by dialysis. The purified product, which was readily soluble in hot water, had mean chain-length 20, by periodate titration and by the reducing-power determination by the method of Blom and Rosted[4]. Its Michaelis constant K_m with β-(soya) amylase at 30° and *p*H 5·8 was compared with that of its parent amylose, and the values expressed as molar concentrations were 5×10^{-5} and $6–8 \times 10^{-5}$ respectively, while the maximum velocities of β-amylolysis were approximately the same.

This is interpreted to mean that there is little or no significant difference between the rates at which the individual long chains of normal amylose and these short ones are hydrolysed by the β-(soya) enzyme. In any event, both kinds of chain are liable to simultaneous attack, and it seems that the same would hold for the chains of the varying lengths actually present in amylose.

Note added in proof by R. H. H. I comment on Dr. Kerr's recent letter[5] without consulting Prof. Jelinek, who is now abroad.

With the first two paragraphs I agree; but consider the evidence offered in support of the 'single-chain' theory to be susceptible to other explanation. Further, the unconverted residues left by β-amylolysis of our short-chain fission product to 50 and 70 per cent gave red iodine colours with absorption values only 60 and 30 per cent, respectively, of those yielded by the fission product, whereas they should be at least 100 per cent if the 'single chain' theory were valid. On the 'multi-chain' hypothesis the observed values were such as to be expected, since a reduction of all chains to a mean length of 10 (and 6) would have occurred.

I picture a 'multi-chain' hydrolysis as described in the letter above, and involving the following successive stages: (1) A reaction of zero order until the shortest chains disappear. DP_n or mean chain-length falls. (2) Molar concentration $[A]$ falls and, with it, reaction velocity (v). (3) When the chains of average length (the majority-law of distribution) are being finished, $[A]$ and v are falling faster, v more rapidly than in a reaction of the first order. DP_n may even rise. This is a long stage towards the end of which short-chain products may be detected against the diminishing quantity of amylose (4) Only the longest chains, now much shortened, remain. $[A]$ and v are low and asymptotically approaching zero. DP_n is falling.

I consider that this picture interprets the known data rather better than Dr. Kerr's, but that the final answer is not yet possible.

R. H. Hopkins
B. Jelinek

Department of Industrial Fermentation,
University,
Edgbaston, Birmingham, 15.
Oct. 12.

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A Tick Resistant to γ-Benzene Hexachloride

The presence of an arsenic-resistant tick, a strain of the one-host blue tick, *Boophilus decoloratus* Koch, was first suspected in the East London district of South Africa in 1938. Proof of this was furnished by Cmer-Cooper and Whitnall[1] in 1945. It now appears that this same strain of tick has also developed a resistance to γ-benzene hexachloride (B.H.C.).

Whitnall and Bradford[2] showed by *in vitro* experiment that γ-benzene hexachloride was extremely toxic to arsenic-resistant ticks, as 50 parts per million (p.p.m.) of the γ-isomer was the highest concentration necessary to inhibit egg-laying. Field results[3] were in line with the laboratory experiments. Larvæ, nymphs and adults were scraped each week for six months from untreated animals, while only very occasionally, after the first four weekly dippings, could a solitary nymph or adult be found on animals regularly dipped in a wash originally containing 50 p.p.m. of the γ-isomer. Furthermore, on one ranch 622 cattle died during the period May 1945 to April 1946, whereas only 69 animals died during the next twelve months when γ-benzene hexachloride dips replaced arsenical dips.

The experiments with ticks have continued over a period of nine years, and during the past four, since the *in vitro* technique was standardized, 50,641 adult female blue ticks have been treated in the laboratory, where freshly mixed dilutions of 50 p.p.m. γ-benzene hexachloride always gave 100 per cent control. But in March 1948 three cases in the East London district were noticed where γ-benzene hexachloride dips were not effective against blue ticks. Some *in vitro* experiments were carried out in which ticks from a presumed 'non-BHC-resistant' district (Alexandria) were tested alongside ticks from a presumed 'BHC-resistant' district (East London). The Alexandria ticks responded readily, treatment in dilutions of a dispersible paste at 56 p.p.m. and 28 p.p.m. γ-isomer giving 100 per cent and 92 per cent control, which is in line with the results obtained in all districts before 1948. These preparations had little effect on ticks from East London, which were treated at the same time and under identical conditions; the control in each case being only 4 per cent. Ticks from both areas treated with water as a control laid normally.

Further experiments during 1948 and 1949, which are still continuing, fully confirm earlier observations. Blue ticks from East London have been compared with the same species from the Fish River area of the Albany district. East London ticks treated in 0·16 per cent As_2O_3, 100 p.p.m. and 500 p.p.m. γ-benzene hexachloride showed only 10 per cent, 0 per cent and 35 per cent control, while the Fish River ticks showed 10 per cent, 100 per cent and 100 per cent. Similar results were obtained with γ-benzene hexachloride from different sources, and in various preparations including emulsions and dispersible powders containing crude benzene hexachloride, and in preparations of the pure γ-isomer. Laboratory experiments further indicated that the East London and Fish River ticks reacted very differently from each other when given the same treatments with other chlorinated insecticides, excepting D.D.T.

In the East London district scrapings were taken from the necks of untreated and sprayed cattle, and over a period of twelve weeks 1,975 larvæ, 1,418 nymphs and 1,298 adults (blue ticks) were scraped from the necks of two untreated animals. Large numbers of each stage were found each week. Over the same period 2,644 larvæ, 905 nymphs and 443 adults (blue ticks) were scraped from the necks of two cattle sprayed weekly with a dispersible paste spray-wash containing 100 p.p.m. γ-benzene hexachloride. In this case also large numbers of nymphs and adults were found each week, indicating that larvæ survived the weekly sprayings.

Ten years ago the arsenic-resistant strain of *B. decoloratus* first appeared in the East London district, and shortly afterwards it became numerous on coastal farms at Bathurst. Field and laboratory experiments which are still in progress indicate that in some localities in the Bathurst district the arsenic-resistant blue tick has also become resistant to γ-benzene hexachloride. Furthermore, it is evident that in these two areas, East London and Bathurst districts, the benzene hexachloride-resistant tick is spreading rapidly. It is remarkable that this new strain of tick has appeared in the same localities as those in which the arsenic-resistant strain first appeared. It is also disquieting that this development should have happened only eighteen months after the first use of benzene hexachloride dips in the field.

This investigation has been sponsored by African Explosives and Chemical Industries, Ltd., and Messrs. Cooper and Nephews (S.A.) Pty., Ltd. We wish to

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A. B. M. Whitnall
J. A. Thorburn
G. B. Whitehead
W. M. McHardy
F. Meerholz

Zoology Department,
Rhodes University,
Grahamstown.
July 4.

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Duration of Protection by Antihistaminics in Anaphylactic Shock

Traina and Aleksandrowicz reported recently[1] that, in contrast to the findings of Pasteur, Vallery-Radot, Halpern and Holtzer[2], guinea pigs which survived a previous exposure to anaphylactic shock during antihistaminic treatment were protected against a second challenging injection of the sensitizing agent given one day later. These experiments were carried out on thirteen guinea pigs, of which two were used for control. The implication of such a result might become extremely broad from the point of view of the mechanism of action of antihistaminic drugs.

We thought it worth while, therefore, to report the results of routine experiments carried out over a period of three years, which included most of the known antihistaminics in clinical use. The number of guinea pigs used in these experiments amounts to about eight hundred. The sensitization consisted in two injections of 0·1 c.c. horse serum, given subcutaneously or intraperitoneally, 48 hr. apart. After eighteen days the animals so sensitized were re-injected intravenously (saphenous vein) with 0·5 c.c. serum. With this technique, 80–85 per cent of the guinea pigs used for control died from anaphylactic shock, while all animals given 5–10 mgm./kgm. of the various antihistaminics tested ('Diatrin', 'Antergan', 'Neo-antergan', 'Benadryl', 'Pyribenzamine', etc.) survived. The re-injection with the sensitizing agent of the treated animals which survived the first shocking dose, one day later, produced fatal shock in the same percentage of guinea pigs as in the untreated control group.

Our findings do not agree with those of Traina and Aleksandrowicz, who used the same animal as we did (guinea pig); but are parallel to those of Vallery-Radot, Halpern and Holtzer, though they used a different animal (rabbit). Our conclusion based on this study is that the protection against anaphylactic shock lasts for the same length of time as the presence of the antihistaminic drug in the organism. On the basis of these relatively simple experiments we do not feel justified, however, in making any statement as to the relationship of the antihistaminic drug to the antigen–antibody reaction or, more generally, to the mechanism of action.

M. Chessin
N. Ercoli

Warner Institute for Therapeutic Research,
113 West Eighteenth Street,
New York City.
July 1.

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Influence of some Inhibitors of Animal Hexokinase on Yeast Hexokinase

The observations of Colowick *et al.*[1] that the hexokinase activity of extracts of brain or muscles from normal animals may be inhibited by the addition of some anterior pituitary extracts in the presence of adrenal cortex extract, and that this inhibitory effect is prevented by insulin, has been confirmed by Reid, Smith and Young[2].

Broh-Kahn and Mirsky[3], and more recently Smith[4] and Stadie and Hangaard[5], have been unable to confirm the second observation of Colowick *et al.*, that extracts of muscles of alloxan-diabetic rats show an alteration of the hexokinase activity when compared to normal controls, which may be reversed by insulin.

Besides the action of anterior pituitary extracts on the hexokinase activity, extracts of spleen (Broh-Kahn and Mirsky[3]) and meningococcal endotoxin (Kun[6]) have been found to exert on muscle hexokinase an inhibitory effect which is reversed by insulin.

In the present investigation, the inhibitory activity of anterior pituitary extract and of the meningococcal endotoxin on yeast hexokinase has been investigated. Of the various extracts prepared by Colowick *et al.*, the aluminium hydroxide adsorbate (procedure 2) has been used. The meningococcal endotoxin was prepared according to Kun[7] from a strain of *Neisseria meningitidis* (Type 1, Jordan) kindly supplied by the Central Public Health Laboratory. The hexokinase was prepared from acetone-dried yeast or fresh yeast, ground with quartz sand and water, and centrifuged in an ordinary centrifuge. The supernatant was then spun in the high-speed head at 16,000 rev. per min. The assays of hexokinase activity were made as described by Colowick *et al.* The composition of the reaction mixture is given in Table 1.

Table 1. Effect of anterior pituitary extract on yeast hexokinase in absence or presence of insulin.
The main compartment of the Warburg vessels contains: 0·5 ml. of 0·04 *M* $MgCl_2$, 0·12 *M* $NaHCO_3$; crystalline insulin (Boots) 200 μgm. in 0·10 ml. *M*/300 HCl or 0·10 ml. *M*/300 HCl; eucortone (Allen and Hanbury) 0·10 ml.; enzyme solution. One side-bulb contains: 0·25 ml. of 0·4 per cent glucose, 0·54 *M* NaF, 0·03 *M* $NaHCO_3$; 0·25 ml. of 0·04 *M* adenosine triphosphate; the other one contains: 0·40 ml. of anterior pituitary extract or 0·40 of 0·1 *M* Na_2HPO_4. Total volume: 2·35; gas, nitrogen + carbon dioxide (5 per cent). Incubation, 10 min. at 30°

Glucose (μgm.) utilized per 2·35 ml. reaction mixture				
With anterior pituitary extract		Control with insulin	Differences in glucose utilization in % of *A*	
No insulin *A*	With insulin *B*	*C*	(*A* − *B*)	(*A* − *C*)
520	529	445	− 1·73	+14·2
339	339	385	0	−13·5
326	333	347	− 2·15	− 6·43
439	401	384	+ 8·65	+12·5
185	185	199	0	− 7·5
409	417	413	− 1·95	− 0·98
347	285	361	+19·3	− 4·0
429	429	425	0	+ 0·93
530	498	534	+ 6·0	− 0·75
458	465	469	− 1·53	− 2·4

Neither the anterior pituitary extracts nor the meningococcal endotoxin in various concentrations from 1 to 3 mgm. dry weight showed any inhibitory effect on yeast hexokinase activity, and, consequently, any influence of insulin could not be demonstrated. The results are summarized in Tables 1 and 2.

Table 2. Effect of *Neisseria meningitidis* endotoxin on yeast hexokinase in presence or absence of insulin. Reaction mixture as in Table 1. One side-bulb contains the endotoxin in various concentrations

Glucose utilized (μgm.)					Differences in glucose utilization in % of *A*	
With endotoxin						
1 mgm.	3 mgm.	2 mgm.		Control with insulin *C*	*A* − *B*	*A* − *C*
		No insulin *A*	With insulin *B*			
519	519	548	519	519	+ 5·3	+5·3
559	578	568	558	548	+ 1·76	+3·5
—	422	360	326	370	+ 9·45	−2·78
—	—	412	365	408	+11·4	+0·97
—	—	515	476	525	+ 7·57	−1·94

In view of the results obtained, the difference in behaviour of yeast hexokinase and animal tissue hexokinase in regard to inhibitors suggests that the two enzymes are not identical. An analogy to the present findings may be found in a previous investigation of Price, Slein, Colowick and Cori[8], who observed that the 'K' fraction of anterior pituitary extract does not exert any inhibitory effect on yeast hexokinase although it does inhibit animal hexokinase.

I wish to express my thanks to Prof. F. G. Young for his advice and criticism.

E. Bonetti

Department of Biochemistry,
University College,
London, W.C.1.
British Council Scholar (1948–49) from the
Institute of General Pathology,
University of Rome.
Sept. 19.

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Failure of Mepacrine Hydrochloride to eliminate Oocysts from the Fæces of Rabbits Chronically Infected with *E. stiedæ*

The proposal to introduce lapinized virus as a prophylactic agent in the control of rinderpest in cattle in Nigeria has raised a number of problems associated with the maintenance of large colonies of rabbits. A survey carried out to determine the incidence of infection with *E. stiedæ* in existing stock showed that one of the most important of these problems would be that of controlling coccidiosis among them. This survey showed that all the forty rabbits examined were passing oocysts in the fæces. As this did not appear to be an entirely satisfactory prelude to the inauguration of extensive breeding activity, it was decided to try the effects of one of our newer coccidiostatic agents, mepacrine hydrochloride, in the treatment of coccidiosis, when this, as in the case of the animals referred to above, had reached the chronic stage.

Mepacrine hydrochloride has been used by a number of workers in the treatment of acute coccidiosis in rabbits, and favourable results have been reported by all. It is now recommended for use in a dose of 10 milligrams per kilogram daily, being administered either in the drinking water or in the food.

The rabbits used in the experiments outlined below were all naturally infected, and were passing small numbers of oocysts in the fæces. Throughout the course of the experiment both treated rabbits and untreated controls were kept in individual cages, which were cleaned out every morning and washed down with a 2 per cent solution of ammonia, which has been shown[1] to be lethal to oocysts. The mepacrine hydrochloride, in doses ranging from 5 to 50 mgm./kgm. daily, was added to the mash upon which the animals were fed. Except in the case of the 5-mgm. dose, which was given wholly in the morning feed, half the prescribed dose was given in the morning and half in the evening feed. The drug was administered for five consecutive days at each dose-level.

As interest centred around the effectiveness of mepacrine in eliminating oocysts from the fæces, rather than in bringing about a reduction in their number, and as the number of oocysts being excreted was small, the zinc sulphate centrifugal flotation technique was employed in the examination of fæces. Fæcal examinations were carried out every morning. The results summarized here are based on more than eight hundred such examinations.

Ten rabbits, known from the results of fæcal examinations carried out over four days prior to the commencement of the experiment to be passing oocysts in the fæces, were given a daily dose of 5 mgm. of mepacrine per kgm. A further seven rabbits were held as controls. Oocysts continued to be discharged in the fæces over the period of five days during which the drug was administered. At the end of this period, the dose was raised to 10 mgm./kgm., and a further five rabbits were added to the group receiving treatment. This procedure was adopted to enable us to observe any tendency to drug fastness on the part of *Eimeria*, should this have occurred. All animals, the fifteen receiving treatment and the seven controls, continued to pass oocysts over the five days during which the drug was administered, and for a period of two days after treatment had been withdrawn. Although no attempt was made to count the oocysts, no obvious decline in the intensity of infection was observed in the treated group as compared with controls.

The experiment was continued in the same group of animals in so far as the evaluation of a dose of 15 and 20 mgm. was concerned. Fresh animals were used in determining the effects of the 30 and 50 mgm. dose. In each experiment control animals were examined concurrently with those treated. Provision for observation of the possible development of drug fastness was made by the inclusion, among the rabbits dosed with 30 mgm. and among those dosed with 50 mgm./kgm., of animals previously given the drug at a rate of 5, 10 and 15 mgm./kgm. and 5, 10, 15 and 30 mgm./kgm., respectively. No indication of its occurrence was observed.

In no instance did mepacrine hydrochloride, administered in any of the doses stated above, bring about the complete disappearance of oocysts from the fæces.

The value of mepacrine hydrochloride in reducing acute infections with coccidia in animals has been

recorded by a number of workers, and there can be no doubt that, used at this stage in the infection, the drug is a valuable addition to the therapeutic agents at our disposal. It is not unusual, however, for a drug which is of proved reliability in acute cases of disease to be found to be of little value once the disease has entered into a chronic phase. The precise cause of this failure in the case of mepacrine hydrochloride is a matter for conjecture. It may be, however, that the thickening of the bile ducts, which is a most noticeable lesion in the liver of rabbits suffering from chronic hepatic coccidiosis, interferes with the ability of the drug to penetrate satisfactorily into the epithelial cells in which the parasites occur.

I am indebted to the Director of Veterinary Services, Nigeria, for permission to publish this note.

K. UNSWORTH

Veterinary Research Laboratory,
Vom, P.O. Bukuru,
Northern Nigeria.
July 5.

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Extraction of Lymphocytes from Rabbits' Blood

WHEN rabbits' blood is defibrinated, the granulocytes, monocytes and platelets adhere to the fibrin fibres and are removed with them. The lymphocytes may then be separated from the red cells by adding dextran[1] or fibrinogen[2] in solution in normal saline to increase the red-cell sedimentation-rate.

Blood from the median ear artery was withdrawn into a test-tube through a cannula with a stab point, and at once defibrinated by twirling in it a glass rod of 1 mm. diameter, bent down the greater part of its length into zig-zag angles so that it just fitted inside. Rapid, even and prolonged twirling is essential.

A solution of dextran in normal saline was then added to the residual suspension of red cells and lymphocytes in serum, to give a final dextran concentration of 1·5 per cent. Erythrocyte sedimentation was complete within a few hours. The supernatant suspension of lymphocytes was withdrawn, and the lymphocytes spun down, washed and resuspended in saline.

Differential leucocyte counts of the defibrinated blood of twenty rabbits were recorded. Eleven of these rabbits yielded values between 95 and 100 per cent lymphocytes. The lowest value was 74·5 per cent. Where blood counts showed a yield of less than 95 per cent lymphocytes, the lower useful limit for most purposes, citrated plasma and excess calcium chloride were added to the defibrinated blood, and the defibrination was repeated.

A second defibrination succeeds in raising to 95 per cent or more a count which had been as low as 85 per cent after a first defibrination. Of the twenty rabbits, only two yielded blood of which the final lymphocyte count lay below the useful range.

The accompanying representative table demonstrates the success of the technique:

Percentage of lymphocytes in the blood leucocytes of six rabbits

	Before defibrination (%)	After defibrination (%)	After second defibrination (%)
(1)	83	100	—
(2)	71·1	98	—
(3)	68	99	—
(4)	65·6	96·4	99
(5)	60	86·3	96
(6)	51·5	74·5	90

Three independent trials gave no evidence that defibrination in any way affects the leucocyte count of human blood. Platelets are, however, removed by this method.

D. M. PICKUP

Department of Zoology,
University of Birmingham.
July 7.

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Absorption Spectra, Molecular Weights and Visual Purple

Collins and Morton[1] have recently compared Houston's equation[2]

$$\varepsilon_{max.} = A \frac{p}{n} \cdot \frac{\lambda^2_m}{\lambda' - \lambda_m} \qquad (1)$$

with Macnoll's[3]

$$\varepsilon_{max.} = B \frac{f}{\nu_m - \nu'}, \qquad (2)$$

where $\varepsilon_{max.}$ is the molecular extinction coefficient at the maximum of an absorption band the wave-length of which is λ_m $(= 1/\nu_m)$; λ' $(= 1/\nu')$ is the wave-length at which the absorption is semi-maximal, A and B are universal constants, n is the refractive index of the solvent at λ_m, and p is the classical oscillator strength; f is given approximately by the expression

$$f = C \times a, \qquad (3)$$

where C is another universal constant, and a is the area included between the absorption curve and the wave-length scale.

Collins and Morton have calculated f for hæmoglobin from equation 2 and found it to be 0·085. They state that this is very far from my assumed value of unity[4]. There are three reasons for this discrepancy. First, I was not referring to equation (2) but to equation (1), saying that in a large number of instances p was of the order of unity in the visible region. Substitution of the appropriate numerical values in these equations reveals, on dividing (1) by (2), that $p = 2 \cdot 7f$. It thus follows that f cannot be unity at the same time as p. Secondly, Collins and Morton divide the observed value of $\varepsilon_{max.}$ by 4, thus further reducing the final value of f. The reason for this division is that the hæmoglobin molecule contains four hæms. It would appear from Svedberg and Brohult's[5] work that this molecule can be considered as one entity: this renders questionable the justification for dividing by a factor of 4. If allowance is made for these two points, the value of $p = 2 \cdot 7 \times 4 \times 0 \cdot 085 = 0 \cdot 92$. The remaining discrepancy is due to Houston's approximation: equation (1) should contain the term $\frac{\lambda_m \lambda'}{\lambda' - \lambda_m}$ if $\lambda = \frac{1}{\nu}$; for a narrow band, however, $\lambda' \lambda_m \approx \lambda^2_m$. The difference between Collins and Morton's value for f and mine for p is thus accounted for.

So far as visual purple is concerned, Collins and Morton hazard the guess that its f value is not likely to be less than 0·84 or greater than 1·92. By combining Broda, Goodeve and Lythgoe's[6] with their

own experimental results, they conclude that the maximum value of the carrier-weight of visual purple is 98,500f. This means that the limits of this value are 83,000 and 197,000. On the other hand, if the value of $p = 1$ is accepted, the maximum value of the carrier-weight is at least 36,400: this is in much better agreement with Broda, Goodeve and Lythgoe's own determination[6] of 26,500. Impurities will affect the former value of 36,400 in two ways: they will increase the density and broaden the band. Only the former of these factors can have affected the result of Broda *et al.*, because it is not based on a measurement of the width of the absorption band. They, too, think that 26,500 is a maximum value and that the true value of the carrier-weight may well compare with the Svedberg unit (17,600).

The above holds only if one accepts the view that the chromophore and not the molecule is to be considered. If, on the other hand, the latter is the basis of the argument, then 36,400 should be the molecular weight of visual purple: by a coincidence, this value lies half-way between Broda, Goodeve and Lythgoe's result for the carrier-weight and mine for the molecular weight (46,000). Impurities present in Collins and Morton's solution would tend to reduce the calculated value, which may well be greater than 36,000.

Collins and Morton have also shown that the number of chromophores per molecule n was related to f by the inequality $f \geqslant 2{\cdot}74/n$, where 2·74 is proportional to the molecular weight of visual purple.

It has been shown above that f should have a value much less than unity if Collins and Morton's result is to compare with that of Broda, Goodeve and Lythgoe. Supposing that f is about 0·25, it follows that n must be 11 or more. This number of chromophores, which is unusually large, considering the type of molecule and the part of spectrum, is solely due to Hecht and Pickels's value[7] of the molecular weight of visual purple (270,000). It has already been criticized as being too large, and it will be noticed that a value of the order of 50,000 would reduce the number of chromophores per molecule to one more commonly met with. In this connexion, Smith and Pickels's[8] work on digitonin should be recalled. This is the detergent used by Hecht and Pickels in the extraction of visual purple. Its molecular weight is 1,228. But the micellar weight, as determined by the use of the ultracentrifuge, is 75,000 and may be as high as 400,000. When this is borne in mind, the value of 270,000 obtained for visual purple by the same method becomes very doubtful. The conflicting data are set out in the accompanying table.

References	Molecular weight of visual purple	Maximum value of carrier weight of visual purple	No. of chromophores per molecule
7	270,000		
6	270,000	26,500	10
1	270,000	83,000–198,000	2–3
4	46,000	26,500	2

Since the publication of the calculations on hæmoglobin and visual purple, my attention has been directed to the fact that Houston's equation gives the right order for the values of the molecular weights of a number of proteins. These calculations are based on the maximum of the band at 0·28 μ, and are, of necessity, only approximate, since other neighbouring bands are known to contribute to the absorption of the principal band. However, the yellow ferment, obtained in a crystalline state by Theorell[9], exhibits a maximum at about 0·38 μ, which appears to be due to a single band. Calculation reveals a molecular weight of 67,000. This supports Theorell's belief that there is only one chromophore present in each molecule: his carrier-weight determination yielded 70,000.

It is thus seen that the empirical device of putting $p \approx 1$ in equation (1) makes it possible to predict the right order of the molecular weights of several substances: it may be possible to account for exceptions as more data become available.

R. Weale

Vision Research Unit,
Institute of Ophthalmology,
(University of London),
Judd Street,
London, W.C.1.
Oct. 14.

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Crystal Structure of Ammonium Tetrametaphosphate

Crystals of ammonium metaphosphate are biaxial, negatively birefringent, with rhombic symmetry $2/m\ 2/m\ 2/m$, instead of tetragonal, as stated by Warschauer[1]. An X-ray investigation showed there are sixteen molecules of ammonium phosphate (NH_4PO_3) in the unit cell with dimensions of 10·40 A., 10·8 A. and 12·75 A. The space group is *Cmca*.

Rotation and Weissenberg diagrams were taken around the axes [100], [010], [001] and [110]. From two-dimensional Patterson projections the probable parameters could be detected. Two-dimensional Fourier projections along [100], [110] and [010] gave detailed information about the atomic arrangement. The parameters in fractions of the cell dimensions are:

		x	y	z
8f:	P_I	0	0·036±0·002	0·150±0·02
8d:	P_{II}	0·211±0·02	0	0
8f:	O_I	0	−0·100±0·004	0·164±0·003
8f:	O_{II}	0	0·121±0·004	0·236±0·003
16g:	O_{III}	0·283±0·004	−0·095±0·004	0·064±0·003
16g:	O_{IV}	0·120±0·004	0·078±0·004	0·075±0·003
8f:	$(NH_4)_I$	0	0·319±0·004	−0·044±0·003
8e:	$(NH_4)_{II}$	0·250	0·272±0·004	0·250

The accuracy of the parameters could be determined by the methods developed by A. D. Booth[2].

As found[3] in the case of aluminium phosphate ($Al(PO_3)_3$) and in the three modifications of P_4O_{10}[4–6], the phosphorus atoms are surrounded by tetrahedra of oxygen atoms; two oxygen atoms of each tetrahedron link the tetrahedra to a ring of four tetrahedra. Thus Warschauer's formula $(NH_4)_4P_4O_{12}$ is confirmed. The P—O distances in one tetrahedron are 1·62 A. for the ring-oxygen atoms and 1·46 A. for the others. The band angles O—P—O are 104° for the ring-oxygen atoms and 122° for the others. The bonds in the P_4O_{12}-ions are resonating between several structures of single and double bonds.

The ammonium ions are surrounded by four oxygen atoms in a slightly deformed tetrahedron with a mean N—O distance of 2·87 A. We may

suppose the presence of weak hydrogen bonds between the ammonium ions and the oxygen atoms.

The P_4O_{12} rings are rather flat, nearly parallel to (010). In agreement with this arrangement the smallest optical refractive index was found parallel to [010]. In spite of this arrangement, no cleavage parallel to (010) was found, the layers being linked very strongly by the ammonium ions.

C. Romers
Laboratory of Physical Chemistry,
University of Indonesia,
Bandung.

J. A. A. Ketelaar
C. H. MacGillavry
Laboratory for General and
Inorganic Chemistry,
University, Amsterdam.
July 12.

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Amino-acid Composition of Bence–Jones Protein

Our knowledge of the amino-acid composition of Bence–Jones protein is still incomplete. Recently, Dent[1] has analysed a specimen of Bence–Jones protein, using paper partition chromatography, with regard to its amino-acid composition. He found that the specimen contained all the common amino-acids except methionine and hydroxyproline. Dent's findings were at variance with those of Devine[2], who found methionine present in amount 0·58 per cent.

In the present studies, the amino-acid composition of two specimens of Bence–Jones protein were investigated by means of paper partition chromatography[3]. The specimens were obtained from the urines of two patients we had under observation for a long period of time. The proteins showed all the characteristics of Bence–Jones protein (reversible heat coagulation, salting out, etc.). Our results were as follows: (1) With the exception of methionine and hydroxyproline, all the common amino-acids were present in the Bence–Jones protein hydrolysates. (2) No attempt at quantitative determination was made. However, from the size of the spots, as well as from the intensity of the colour reaction with ninhydrin on the chromatogram, it could be concluded that aspartic and glutamic acids, cystine and tyrosine were in high concentration, whereas lysine and serine were in low concentration.

Examination for methionine was made, apart from the ordinary chromatographic procedure of Consden *et al.*[3], by using its catalytic effect on the iodine–sodium azide reaction. The technique consisted in extracting the amino-acid from the corresponding area of the filter paper, with subsequent procedure suggested by Feigl[4] for the detection of organic sulphur compounds. The method was very sensitive; amounts of methionine not exceeding 1 μgm. could readily be detected.

The above findings confirm Dent's data and offer further support for his suggestion that Bence–Jones protein is an abnormal protein foreign to the animal body. Again, the results are not in conflict with Waldenström's theory[5] of the virus origin of myelomatosis.

S. C. Papastamatis
J. E. Kench
John F. Wilkinson
Department of Hæmatology,
Royal Infirmary,
Manchester 13.
July 9.

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Production of Kojic Acid from *Aspergillus lutescens*

Jennings and Williams[1] directed attention to the fact that kojic acid is a common product of fungus metabolism and may account for the antibacterial properties of a number of fungi not yet investigated. They further pointed out that the ferric chloride colour test for this substance is not specific. However, since kojic acid must be present in fairly high concentration if it is responsible for an inhibitory effect with, for example, the cylinder-plate test, it can usually be obtained in crude crystalline form by allowing an ether extract of crude culture fluid, made at about *p*H 5, to evaporate.

D. E. Gill-Carey[2] recently found that *Aspergillus lutescens* Bainier *nomen nudum*, No. *NRRL* 425 in the collection of the Northern Regional Research Laboratory, Peoria, and No. 4640.478 in Dr. Charles Thom's collection, produced antibacterial activity when grown on various media. The whole of this activity has now been shown to be accounted for by the presence of kojic acid, which was isolated by the procedure just mentioned. The best yield was obtained by growing the organism on 5 per cent malt extract, *p*H 6·0, containing separately sterilized calcium carbonate, at 24° C. for nine days.

After recrystallization from acetone, the identity of the material was established by melting point and mixed melting point with authentic kojic acid.

Robert Q. Marston
Sir William Dunn School of Pathology,
University of Oxford.
July 9.

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Phosphorus Content of Ovalbumin and of some Products of its Enzymatic Degradation

As is well known[1,2], the phosphorus content of ovalbumin does not, in general, correspond to an integral number of phosphorus atoms per mole of this protein if its molecular weight is taken as 44,000. About two years ago, Linderstrøm-Lang suggested to me that this lack of stoichiometry might be correlated with the occurrence, in ovalbumin, of two electrophoretically distinguishable components, A_1 and A_2[3], the relative abundance of which varies somewhat from one preparation to another but averages about 85 per cent A_1 and 15 per cent A_2. In the course of the electrophoretic studies carried out

Incubation at 37° C. (days)	Crystal form	Concentrations of electrophoretic components (per cent)					% Non-protein nitrogen	Mgm. phosphorus per gm. nitrogen	Atoms phosphorus per mole protein	
		A_1 (−5·9)	A_2 (−4·8)	P_1 (−5·5)	P_2 (−4·4)	Q (−3·6)			Observed*	Calculated from electrophoretic data
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
0	Needles	83·4	16·6					8·2$_9$	1·8$_5$	1·8$_5$
14	Plates			84·1	15·9		1·2	8·2$_9$	1·8$_5$	1·8$_4$
17	Plates			43·4	41·5	15·1	15·7	5·4$_9$	1·2$_4$	1·2$_5$
20	Plates			29·7	52·3	18·0	21·0	5·1$_9$	1·1$_4$	1·1$_2$
26	Plates			16·1	57·2	26·7	37·7	4·1$_0$	0·9$_1$	0·8$_5$
36	Plates			10·8	56·6	32·6	51·0	3·9$_0$	0·8$_7$	0·7$_6$

* Evaluated from the data of col. 9, assuming a protein molecular weight and nitrogen content of 44,000 and 15·76, respectively.

in this laboratory of the ovalbumin → plakalbumin transformation recently discovered by Linderstrøm-Lang and Ottesen[4–6], a modification of ovalbumin was encountered which crystallized in plates but differed electrophoretically from plakalbumin[7]. The solution from which these plate crystals were obtained was found to be contaminated with Gram-positive, rod-shaped bacteria, probably *B. subtilis*. In subsequent experiments a subculture from a single colony of this bacterial contaminant was kept in blood broth as the stock culture and was used as a source of enzymes for modifying ovalbumin. Phosphorus analyses of the proteins at different stages of enzymatic degradation were made. A comparison of these results with the electrophoretic analyses has made possible a test of Linderstrøm-Lang's suggestion.

The experimental procedure can be described in conjunction with the results summarized in the accompanying table. A sample of freshly prepared salt-free ovalbumin, having the composition given in line 1, cols. 3 and 4, and a phosphorus content shown in col. 9, was inoculated with a loop-full of freshly prepared broth culture. Aliquots were removed, at the times given in col. 1, for analyses, the results of which are reported in the corresponding line of the table. Most of the protein in each aliquot could be crystallized, and the crystal form is stated in the second column. On incubation of the solution at 37° C., a definite lag period was observed during which no changes of the ovalbumin occurred. The protein in the aliquot taken after 14 days incubation, however, crystallized in plates and had the same phosphorus content as the starting material. Since the non-protein nitrogen (col. 8) corresponded closely to that observed by the Danish workers for the ovalbumin → plakalbumin transformation[4–6], it may be concluded that at this stage the protein is present as essentially 'pure' plakalbumin, P. As previously noted[8], the reactions $A_1 \rightarrow P_1$ and $A_2 \rightarrow P_2$ appear to proceed at about the same rate and are accompanied by mobility changes that can be correlated with the loss of a glutamic and possibly aspartic acid residue in the $A \rightarrow P$ process. The components of the mixtures A_1, A_2, P_1, P_2 and Q are identified in the table on the basis of their mobilities, the values of which in a 0·1 ionic strength sodium phosphate buffer at *p*H 6·8 are given in parentheses. The validity of this identification has been checked in several instances by electrophoretic resolution of appropriate synthetic mixtures of the components.

On continued exposure to the bacteria, a component, Q, of low mobility appears in the patterns, and the percentage of non-protein nitrogen progressively increases while the protein phosphorus decreases. The lost phosphorus is recovered quantitatively in the non-protein fraction as inorganic phosphate. It is suggested that these effects may be due to the presence of other enzymes, which produce changes of the protein different from that responsible for the $A \rightarrow P$ process. It is clear that at least one phosphatase is included among these enzymes. Throughout this degradation, however, the residual protein remains crystallizable as plates. Moreover, the Q component is reasonably homogeneous electrophoretically. These observations suggest that Q is simply dephosphorylated plakalbumin, and that this dephosphorylation occurs before essentially complete degradation of plakalbumin by the non-specific proteolytic enzymes takes place. It is also clear now that the modification of ovalbumin originally observed in the contaminated solution[7] had proceeded somewhat beyond the plakalbumin stage.

If now the assumption is made that both A_1 and P_1 contain two atoms of phosphorus per mole of protein, A_2 and P_2 one atom per mole and that Q contains no phosphorus, the phosphorus content of each preparation listed in the table can be computed with the aid of the electrophoretic analyses. The values thus computed (col. 11) are in excellent agreement with the actual determinations (col. 10), and afford a confirmation of Linderstrøm-Lang and Ottesen's hypothesis regarding the phosphorus content of ovalbumin[6]. Moreover, if the phosphorus is present in the protein as a negatively charged phosphate group, the loss of this charge on dephosphorylation should decrease the anodic mobility and, as can be seen from the table, this is observed experimentally. It is thus possible that the main difference between A_1 and A_2 and between P_1 and P_2 is in the group containing the phosphorus.

Work on a more direct test, namely, the phosphorus content of purified A_1 and A_2, is in progress; but the fractionation is proving to be a difficult one. The following observations have been of value throughout this work: preparations of ovalbumin have been stored as a paste under saturated ammonium sulphate at 3° for as long as eight years without a change in the electrophoretic pattern or of the phosphorus content. If a salt-free, isoelectric ovalbumin solution is sterilized by filtration through a 'COORS' bacteriological filter, it also can be stored unaltered with respect to its electrophoretic composition and its protein phosphorus. However, in the case of salt-free solutions, toluene is inadequate as a preservative. Solutions stored in this manner frequently become infected, and enzymatic changes occur which are similar to those here reported. It is quite possible that the changes observed by MacPherson, Moore and Longsworth[9] were of this type, and that the $A_1 \rightarrow A_2$ transformation described by them actually involved proteolysis and dephosphorylation as in the present case.

I wish to express my sincere thanks to Prof. K. Linderstrøm-Lang for valuable criticism, to Dr. L. G.

Longsworth for help in preparing this manuscript, and to Dr. R. C. Lancefield for her advice throughout this investigation.

GERTRUDE E. PERLMANN
Rockefeller Institute for Medical Research,
New York.
July 8.

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Use of Pyridine in the De-ionization of Solutions for Paper Chromatography

Partridge[1] and Westall[2] have stressed the need for the complete removal of electrolytes in preparing solutions for paper chromatography when the subsequent development of the chromatogram involves the use of ammoniacal silver nitrate. The use of ion-exchange columns—'Zeo-Karb 215' and 'Deacidite E'—for this purpose in the routine analysis of dilute solutions of sugars in Ringer phosphate incubates proved slow and uncertain in our hands. The following procedure, however, based on the solubility of sugars and the insolubility of inorganic salts in pyridine, has given a consistent elimination of salt effects in our chromatographic studies, and is well suited to routine investigations.

The solutions to be examined (in our work the volumes were about 5 ml.) are dried on a boiling-water bath and the residues extracted with dry, redistilled pyridine (5 ml.) for 10 min. at 100° C.; any solid adhering to the sides of the vessels is ground into the pyridine with a glass rod. The stoppered solutions are allowed to cool and then filtered from the salt residue. The pyridine is removed by distillation under reduced pressure at a temperature not exceeding 40° C., and the residue containing the sugar is dissolved and washed from the flask with the minimum volume of water and afterwards suitably concentrated for application to the paper. Under these conditions we have observed no loss of sugars such as was found by Jermyn and Isherwood[3] when heat-drying paper chromatograms prepared with ethyl acetate–pyridine–water mixtures, processed solutions giving reduction spots of intensity comparable with those from standard untreated control solutions of the same strength.

The method has proved most useful in demonstrating the formation of lactose from glucose and glycogen in *in vitro* studies on incubates of mammary gland tissue. The full results of this work will be reported elsewhere.

F. H. MALPRESS
A. B. MORRISON

Department of Biochemistry,
Queen's University,
Belfast.
July 12.

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Interaction of Iodine with Aromatic Hydrocarbons

A RECENT communication by Bayliss[1], commenting upon the spectroscopic evidence for specific, 'chemical' interaction between iodine and benzene obtained by us[2], quite properly includes the remark that such spectroscopic evidence should be "interpreted with caution", and he advanced a formula for the shift of the ultra-violet absorption band of iodine toward the red in terms of its polarizability, dipole-strength, and the refractive index of the solvent. We ourselves, at the outset of our investigation, were prepared to find the influence of the solvent to be general or physical rather than specific; but the evidence we obtained later[3] has all been in favour of a definite 1 : 1 molecular complex. Excellent constancy was obtained for the constant of the equilibrium, $I_2 + A \rightleftharpoons I_2.A$ in a "violet' (neutral) solvent, where A denotes an aromatic hydrocarbon. Moreover, the interaction is stronger in the case of the more basic mesitylene than in benzene, whereas, according to the formula of Bayliss, it should be weaker.

We have recently determined the solubility of iodine in mesitylene and find it to be greater than in any other solvent (on a mole fraction basis), and that the enhancement over what would be expected for a regular solution is in good accord with the degree of chemical interaction deduced from the spectral data. Finally, the entropy of solution, as revealed by the temperature coefficient of solubility, is very different from the regular solution entropy.

JOEL H. HILDEBRAND
HANS A. BENESI

Department of Chemistry,
University of California,
Berkeley, California.
Sept. 28.

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Toxic Action of some Simple Gases at High Pressure

IN the course of an extended study of the action of 'physically toxic' substances[1] on the grain weevil, *Sitophilus granarius*, we have determined for this organism the median lethal doses of a number of simple gases such as hydrogen, nitrogen, argon, etc. To attain the required lethal concentrations in these cases, it was necessary to apply the gases at pressures much above atmospheric—for example, up to almost 900 atmospheres in the case of hydrogen.

The L.D.50 values were determined by exposing the insects, in batches of 100, to the action of the compressed gases in a bomb of 200 c.c. capacity, containing also air at a partial pressure of one atmosphere. The time of exposure at each pressure tested was 5 hr., excluding the periods required to compress and decompress the insects; these latter periods were roughly proportional to the logarithm of the final pressure attained, and did not, for the highest pressures used, exceed twenty minutes. The temperature was maintained at 25° C. The numbers of survivors were counted after recovery periods of seven days. A minimum of five points was used to construct the probit-log dose curve from which the L.D.50 values were obtained by inspection.

The results so far obtained, with, for comparison, some earlier results on the toxicities of substances lethal at low partial pressures[1], are given below:

Substance	B.P. °C.	Toxic partial pressure	L.D.50 gm. mol. × 10^{-6}/litre	'Activity'
Hydrogen	−252·8	850 atm.	22,000,000	—
Nitrogen	−195·8	340 ,,	12,000,000	0·28
Oxygen	−183·0	13 ,,	530,000	0·02
Methane	−161·5	180 ,,	8,800,000	0·53
Argon	−185·7	92 ,,	3,900,000	0·10
Ethylene	−103·9	15·5 ,,	700,000	0·31
Nitrous oxide	−89·5	14·5 ,,	640,000	0·36
Ethane	−88·3	11·5 ,,	520,000	0·37
Ethyl chloride	12·2	330 mm. Hg.	17,000	0·29
Chloroform	61·3	40 ,,	2,100	0·20
Ethylene dichloride	83·6	19 ,,	1,000	0·24
Sym-Tetrachlorethane	146·3	1·7 ,,	90	0·24

It is clear from this table that hydrostatic pressure, *per se*, is not the cause of death, since the lethal pressure varies with the gas used.

The fifth column of the table gives the values of the thermodynamic activities (see ref. 2) of the various substances at the L.D.50 concentration. In each case this is the ratio of the fugacity of the toxic concentration to that of the saturated vapour of the substance at the temperature of the experiments, namely, 25° C. The permanent gases in the table are, of course, above their critical points at 25° C. A fictitious saturated vapour pressure was calculated for each of these cases by extrapolating the vapour pressure curve above the critical temperature in accordance with the procedure adopted in solubility studies by, for example, Hildebrand[3]. Fugacities were then estimated using activity coefficients obtained from critical data[4]. No figure is given for hydrogen as the extrapolation required is too great.

It will be seen that the toxic activities or 'thermodynamic concentrations' in column 5—with the exception of the value for oxygen—are roughly constant. This is to be contrasted with the very great molar concentration range (130,000-fold between nitrogen and tetrachlorethane). This observation, and also the fact that the inert gas, argon, is toxic—and toxic at a lower molar concentration than several other gases—is readily explicable on the view that, apart from oxygen, the substances listed in the table act on the grain weevil by a 'physical' mechanism[2]. On the other hand, the low value of the activity value for oxygen indicates that under the conditions used it acts as a 'chemical' poison.

The rough constancy of the toxic activity values in column 5, apart from that for oxygen, would suggest, similarly to the concepts of the lipoid theory of narcosis, that all the physically toxic substances listed here exercise the same primary effect in the sensitive biophase at real concentrations of roughly the same order of magnitude. To attain the effective concentration it is necessary to use markedly different external concentrations of the various substances, because of their very different biophase/external phase partition coefficients. At pressures much lower than the L.D.50 value, the insects were simply narcotized and all recovered after exposure. Death at higher pressures is presumably due to secondary effects, following prolonged and intense narcosis.

In this connexion, it should be remarked that Meyer and Hopff[5] have produced reversible narcosis of mice and other animals by the application of nitrogen at 90 atmospheres partial pressure and of methane at 3·7 atmospheres. Behnke[6] and Behnke and Tarbrough[7] observed narcosis in human subjects exposed to argon at a partial pressure of 8 atmospheres. Lawrence, Loomis, Tobias and Turpin[8] produced pronounced narcotic effects in mice with partial pressures of xenon less than one atmosphere.

J. Ferguson
S. W. Hawkins

Research Department,
I.C.I. (Alkali Division),
Northwich.
July 14.

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Line-Broadening in Solar Flares

In *Nature* of August 13, Bruce[1] contrasts the Zeeman effect and Stark effect as rival causes of line-broadening observed in the spectra of solar flares, and points out that Ellison's own observation, namely, that $H\alpha$, $H\beta$, etc., show smaller widths than $H\gamma$, contradicts the Stark effect hypothesis favoured by Ellison. He argues that the above observation supports the Zeeman effect hypothesis of the broadening of lines in flare spectra. Ellison, in reply, contends that arguments based upon the relative widths of $H\alpha$, $H\beta$, etc., in emission are to be regarded as inconclusive at present on the ground that these lines have not yet been photographed simultaneously in flares.

We give below an observation of the widths of $H\alpha$ and $H\beta$ in a flare spectrum, which does not suffer from a lack of simultaneity. On October 3, 1949, a fairly intense flare occurred slightly to the south of the principal spot of the group at mean lat. 7° N. and long. 52° E. The flare reached its maximum intensity between 3h. 20m. and 3h. 25m. G.M.T. and was observed at Kodaikanal during this period through a prominence spectroscope and a spectrohelioscope by independent observers, who were not aware of each other's proceedings. With the prominence spectroscope, the widths of $H\alpha$ and $H\beta$ were estimated alternately several times, and it was found that the maximum width of $H\alpha$ was 8 A. and that of $H\beta$ 6 A. Although attention was confined mainly to $H\alpha$ and $H\beta$, several other lines were seen in emission; these were D_2, 6,678, D_1, D_2, b_1, b_2, b_3 and b_4, and of these only D_3 showed a width of 1 A., whereas the rest showed no perceptible widening. The spectrohelioscope of this Observatory has recently been fitted with a camera, which permits of photographing $H\alpha$ in the second order of the grating simultaneously with the visual observation of $H\alpha$ in the first order; the spectrohelioscope observer succeeded in securing a photograph of $H\alpha$ during the maximum phase of the flare, and the width of the line as measured on this plate was also 8 A.

The above observations were made under excellent sky conditions, and there can be scarcely any doubt

that in this particular flare the widths of $H\alpha$ and $H\beta$ in emission were, in fact, 8 A. and 6 A. respectively during the maximum phase. These widths are clearly inconsistent, even qualitatively, with the Stark effect hypothesis of line-broadening in flare spectra; but in this particular instance neither does the Zeeman effect fare any better quantitatively as a rival hypothesis. Incidentally, it will be noticed that the above widths are consistent with what is to be expected on the basis of the Doppler effect, although there are certain difficulties in unreservedly admitting this hypothesis without qualification also; in any event, with the meagre observational data so far available, it does not seem justifiable to rule out completely the Doppler effect as a possible major factor.

N. R. Rao
A. K. Das
H. Ananthakrishnan
K. C. A. Raheem
K. Sethumadhavan

Solar Physics Observatory,
Kodaikanal, India.
Oct. 8.

Nature, **164**, 280 (1949).

Those who are interested in the flare problem will welcome observations of the kind referred to in the preceding letter. At the same time, I cannot agree with Dr. Das and his colleagues in their facile conclusion that the measured line-widths of 8 A. and 6 A. for $H\alpha$ and $H\beta$ in emission "are clearly inconsistent, even qualitatively, with the Stark effect hypothesis of line-broadening in flare spectra". After all, these measures merely confirm my own observations, to which both Mr. C. E. R. Bruce and the present writers have referred. For the following reasons it seems improbable that this issue can be decided by line-width measures alone.

We must recollect that flare emission lines are normally observed and photographed in association with the Fraunhofer spectrum of the reversing layer: in the case of hydrogen, therefore, each line is a complex blend of an emission line superimposed upon the absorption profile of the corresponding Fraunhofer line. There is also a good deal of evidence that the emission lines originate, in general, at a level somewhat above that of the reversing layer. The line-width measured at Kodaikanal is therefore what I have called the "effective line-width", as measured between the "extinction points"[1], where the emission profile blends into the wings of the absorption line on the two sides of the line centre. It is by no means certain that this is the same thing as a measure of the total width of the emission line as it would appear if it were freed from blending with the Fraunhofer spectrum. Only on the rare occasions when an intense flare is seen at the sun's limb and detached from the chromosphere can these ideal conditions be realized.

Furthermore, the emission lines decrease in central intensity and the absorption lines decrease in breadth as we pass from $H\alpha$ to the higher members of the series. In these circumstances we should scarcely expect the Stark effect to manifest itself in accordance with the idealized hydrogen patterns for uniform field, such as we find in text-book illustrations. That is to say, we should not look for a progressive widening of the emission wings in the direction $H\alpha$, $H\beta$, etc. There will almost certainly be a blending and a blurring of the transverse and longitudinal Stark components, corresponding to a wide range of field-strengths, and these wings will be combined in the same profile with a strong central core of the unresolved line. Taking these various factors into account, I should say it is by no means clear that the observed values are necessarily inconsistent with the operation of the Stark effect. We need some information on the line profiles and degree of polarization as well.

I may add that the evidence favourable to the Stark mechanism and contrary to the theory of thermal Doppler broadening has been given elsewhere[2]. Briefly stated, there are strong grounds for assuming that there is a sufficiently high concentration of electrons in the flare region for the Stark effect to operate. On the other hand, thermal Doppler broadening would require a temperature of the order 10^6 degrees K. to explain the great line-widths which have been repeatedly photographed and measured[3]; but the flare spectrum is essentially one of low temperature. The matter has been reviewed by F. Hoyle in his book "Some Recent Researches in Solar Physics" (p. 93).

In conclusion, it seems unlikely that we shall be able to shed more light upon this issue until we are in possession of calibrated plates showing a considerable portion of the Balmer series in emission during the 'flash' phase of an intense flare. It will then be possible to examine not merely the widths but also, and more important still, the intensity profiles of the lines. Anyone who can secure such results from a major flare at the sun's limb is assured of a rich reward for his preparedness.

M. A. Ellison

Royal Observatory,
Edinburgh 9.

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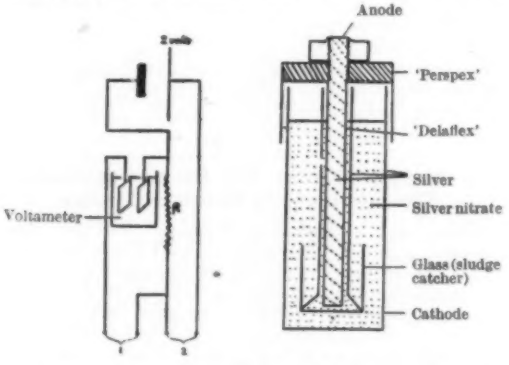
A Simple Device for Recording Mean Temperatures in Confined Spaces

For many ecological and phenological purposes, records of maximum, minimum and mean temperatures are required, while in physiological studies of metabolic-rates only the last-named may be necessary; but in both cases measurements must frequently be made in very confined spaces. Apart from expensive thermocouple amplifiers with their considerable power demands, existing temperature-recording methods are unsuitable for two reasons: the normal thermograph has a sensitive element which is much too large in relation to the spaces of which the temperature is to be measured, quite apart from measuring temperature gradients within such spaces; and, secondly, the process of 'integrating' the curve of a thermograph chart is time-consuming and often inaccurate. My ecological studies require a knowledge of the mean temperature at which soil animals are living, so that laboratory measurements of metabolic-rate may be extended to field conditions; temperatures have therefore to be measured at a number of depths in the soil. At the same time it is desirable for this particular purpose that the values obtained should be related to the temperature not on a linear scale, but in approximately the same way as metabolic-rates are related to temperature, namely, logarithmically, so that a 10° C. increase in temperature has double the effect on the final value, while a 10° C. decrease in temperature

has half the effect of maintaining the apparatus at the mean temperature itself. It should be noted that this second characteristic is not an essential feature of the device. The apparatus used incorporates Type *F* thermistors (manufactured and kindly supplied by Standard Telephones and Cables, Ltd.), a 2-volt accumulator and a silver voltameter connected as shown in the diagram. Mean temperature is calculated from the gain in weight of the voltameter cathode. The curve relating the current flowing through a thermistor to temperature is governed by the formula

$$E/I = a \exp(b/t),$$

where E is applied E.M.F., I is current, t is absolute temperature, and a and b are constants. But the slope of the curve produced when the logarithm of the current is plotted as abscissa against temperature as ordinate is steeper than that relating metabolic-rate to temperature. However, by feeding a voltage proportional to this current to a second thermistor maintained at the same temperature as the first, the resulting current through the second thermistor alone varies more with temperature. By making the resistance R (see diagram) equal to the working mean thermistor resistance, a less steep curve than the metabolic-rate one can be obtained, while, by suitably adjusting this resistance, the combination can be made to conform to the same law as that which governs metabolic-rate. (Similarly, by suitable combinations of thermistors and resistors, almost any logarithmic law can be simulated.) In practice, an apparatus containing three sets of two probes is used with provision for testing for open circuits and leaks.



The accumulator is discharged to approximately a fifth of its capacity and then acts as a voltage source sufficiently constant for the limits of accuracy aimed at (0·1° C.) and the low discharge-rate of about 6 milliamp. The value of the resistance R is determined empirically, using three water-baths at constant temperature; this is necessary because the characteristics of thermistors, although stable, vary considerably from one to another. The main practical difficulty has been the development of a satisfactory voltameter meeting the demands of low resistance, immunity from the effects of chemical reaction, evaporation, loss of the large silver crystals which result from the slow rate of deposition and contamination with anode sludge. The pattern finally used is illustrated; the outer silver cathode is detached and weighed, and the mean temperature during periods of one or two weeks obtained from calibration charts. Experiments with direct-reading mercury voltameters were unsuccessful.

When tested in constant-temperature chambers, the apparatus proved accurate within the limits of normal laboratory thermometers; when compared with a continuous recording thermograph the same results were obtained; the apparatus appears to be giving satisfactory results in the field. There seems to be no reason why its use should not be extended to give maximum and minimum readings by the inclusion of a simple meter device.

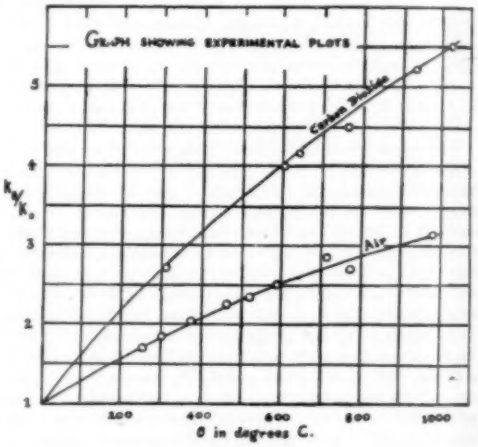
AMYAN MACRADYEN

Bureau of Animal Population,
91 Banbury Road,
Oxford.
July 11.

Effect of Temperature upon the Thermal Conductivity of Gases

I HAVE measured the thermal conductivities of air, nitrogen and carbon dioxide over the temperature range 0–1,000° C. by a simple hot-wire cell system, employing a platinum wire contained in a transparent fused quartz tube. Temperatures were determined from the resistance of a platinum thermometer wound directly on to the wall of the tube.

The apparent gas conductivities were determined from plots of increase in resistance of the hot wire against the square of the current it carried. Calculation of the radiation and wire equivalent conductivities led to the evaluation of the real conductivities of the gases.



The largest end-losses occurred with carbon dioxide, amounting to 18 per cent of the total dissipated power at 0° C., and to 8 per cent at 1,030° C. Similarly, the maximum radiation correction applied at the latter temperature was 21 per cent of the total dissipated power.

It was found that the variation of conductivities (k), with temperature (θ), could be expressed by the empirical relation,

$$k_\theta = k_0 (1 + a\theta + b\theta^2 + c\theta^3),$$

where the constants had the following values.

	Air	Nitrogen	Carbon dioxide
$k \times 10^7$ in C.G.S. units	584	577	357
$a \times 10^3$	3·23	3·13	6·20
$b \times 10^6$	−1·33	−1·33	−2·00
$c \times 10^{10}$	2·33	2·63	2·50

The values of the conductivities at 1,000° C. were calculated to be 183, 176, 195 × 10^{-6} c.g.s. units, for air, nitrogen and carbon dioxide, respectively.

Archer[1] and Sherratt and Griffiths[2] have measured k for carbon dioxide up to the neighbourhood of 350° C., and Milverton[3] determined the variation of k for air over the range 0–100° C. These investigations provide the only data for comparison with my results. For these limited ranges, good agreement is found with Sherratt and Griffiths, and Milverton, but not with Archer.

Air and nitrogen satisfied a Sutherland type of relation over the range 0–600° C.; but above this temperature no agreement was found with any of the normal types of viscosity-temperature relations.

Evaluation of the numerical factor f in the Chapman–Enskog equation, $k = f\rho c_v$, led to the conclusion that only at temperatures above 500° C. did it tend to decrease, but then not so rapidly as predicted by the Eucken theory.

It should be noted here that, apart from the investigations cited above, only the work of Gregory[4] on hydrogen provides direct experimental results for gas conductivity measurements as high as 300° C.

This work formed part of that for a thesis approved by the University of London for the degree of Ph.D. I wish to thank Prof. H. Spencer Gregory for his interest and help.

D. W. Stops

Physics Department,
Imperial College of Science and Technology,
London, S.W.7.
July 18.

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Image Force in Rectifiers

Theoretical current-voltage characteristics of copper oxide and selenium rectifiers have been obtained by integrating the so-called diffusion equation[1]. The result so obtained involves the distribution of the potential of the current carriers in the semi-conductor. In general, this rises to a maximum near the interface between the semi-conductor and the rectifying electrode, and then decreases towards the metal in virtue of the image force $e^2/4kx^2$ (k is dielectric constant of the semi-conductor), which acts on a current carrier in the semi-conductor when it is close to the metal electrode. With increasing applied reverse potentials this maximum is lowered, thus producing the increase in reverse current density which is familiar from known experimental characteristics. The potential due to the image force is additional to a potential distribution which arises from the physical nature of the barrier region. The case of an insulating barrier[2], the case of a barrier containing a uniform distribution of spontaneously ionized impurity centres[3], and a combination of the two[4,5] have been treated neglecting the space charge due to the current carriers; the insulating barrier has also been studied[6] with proper allowance for the space charge due to the current carriers. Only in ref. 2, however, has a theoretical characteristic been given which incorporates the effect of the image force. A general method of taking into account the image force is proposed here, and the results are applied to the copper oxide rectifier.

Let the distance, x, be measured from the interface between the rectifying electrode and the semi-conductor, away from the metal, and let potentials be measured from the potential in the interior of the semi-conductor in the absence of an applied voltage. With this convention the metal is approximately at zero potential, except for a small energy difference which is equal to half the activation energy of the impurity centres. Let the applied voltage U, and the current density j, be positive when acting in the negative x-direction (the forward direction for positive current carriers). Let $N(x,U)$ be the volume density, v the mobility of the current carriers, and W the 'temperature potential' kT/e. If $V(x,U)$ is the potential at the plane with co-ordinate x when the applied voltage is U, then the diffusion equation is

$$j = ev(N\,dV/dx + W\,dN/dx). \qquad (1)$$

This expression will be integrated from the plane $x = a$, situated between the potential maximum and the metal electrode, at which the potential has dropped to zero due to the image force, to the plane $x = d$, at which the barrier ends. Hence $V(a,U) = 0$ and $V(d,U) = U$. The volume density of current carriers $N(d,U)$ at the end of the barrier is equal to the volume density (n, say) of ionized impurity centres in the interior of the semi-conductor, and $N(a,U)$ is equal to the volume density of current carriers in the semi-conductor very close to the metal electrode.

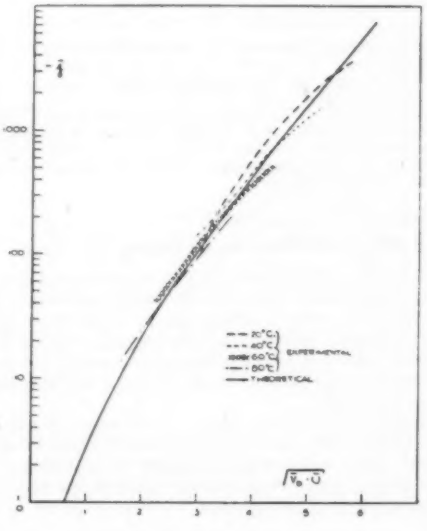
Both these quantities may be taken as approximately independent of the applied voltage, and the integration then yields

$$(j/evWn)\int_a^d \exp\,(V/W)dx = \exp\,(U/W) - 1. \qquad (2)$$

An equation of this type was first derived and discussed by Schottky[3]. Denoting by $x = b$ the co-ordinate of the plane at which the potential is a maximum, it is convenient to use Laplace's approximation

$$[-2\pi W/V''(b,U)]^{1/2} \exp\,[V(b,U)/W] \qquad (3)$$

for the integral on the left of (2). The differentiation V'' is with respect to x. The approximation (3) fails



for the higher temperatures, for forward potentials, when the image force can in any case be neglected, and for high reverse potentials which depress the maximum potential $V(b,U)$ to a value of the order of the temperature potential W.

For Mott's barrier[2] and reverse currents, the characteristic

$$-\bar{j} = (\overline{V}_D - \overline{U})^{3/4} \exp\,[\,(\overline{V}_D - \overline{U})^{1/2}] \qquad (4)$$

is obtained. Currents and potentials are here expressed in the units

$$j_0 = (2/\pi)^{1/2} k W^2 v n \exp(-V_D/W) \text{ and } V_0 = kdW^2/e \qquad (5)$$

respectively, and the characteristic is plotted in the accompanying figure. V_D is the maximum potential in the absence of the image force. Comparison has been made with the characteristics of copper oxide rectifiers[7], using $V_D = 0{\cdot}5$ volt. With $j_0 = 0{\cdot}45$ μamp./cm.^{2} and $V_0 = 0{\cdot}67$ volt, a good fit is obtained at 20° C. Using $v = 40$ cm.^{2}/volt-sec. and $k = 10$, these constants yield the reasonable values

$$d = 1{\cdot}54 \times 10^{-5} \text{ cm.} \quad \text{and} \quad n = 10^{15} \text{ cm.}^{-3}$$

for the copper oxide rectifier. Neglecting the variation of mobility with temperature, the constants (5) may now be calculated for other temperatures:

	20° C.	40° C.	60° C.	80° C.
j_0 (μamp./cm.^{2})	0·45	1·89	6·41	19·6
V_0 (volts)	0·67	0·76	0·87	0·97

Using the calculated values for the three last temperatures, the four experimental graphs can be plotted in the form shown in the figure.

The graphs confirm with some accuracy the prediction of the theory that, expressed in the proper units, the reverse characteristics should have the same form (4) at all moderate temperatures.

I am indebted to Dr. E. Billig of this Laboratory for his helpful comments. More detailed applications of the present calculations to Schottky's theory of rectification and to current carrier distributions in rectifying contacts will be published in due course.

P. T. Landsberg

Research Laboratory,
Associated Electrical Industries, Ltd.,
Aldermaston Court,
Aldermaston, Berks.
July 12.

[1] Mott and Gurney, "Electronic Processes in Ionic Crystals" (Oxford, 1940).
[2] Mott, N. F., *Proc. Roy. Soc.*, A, **171**, 27 (1939).
[3] Schottky, W., *Z. Phys.*, **118**, 539 (1942).
[4] Bethe, H. A., M.I.T. Radiation Laboratory Report 43/12 (1942).
[5] Billig, E., and Landsberg, P. T., *Proc. Phys. Soc.* (in the press).
[6] Fan, Y., *Phys. Rev.*, **74**, 1505 (1948).
[7] Williams, A. L., and Thompson, L. E., *J. Inst. Elect. Eng.*, Pt. 1, **88**, 353 (1941), Fig. 4.

Effect of Rain in Calming the Sea

In *Nature* of August 20, p. 320, a letter appeared giving details of experiments which indicated that falling drops, which strike the surface of water at their terminal velocity, do not produce vortex rings in the water. I have, however, recently performed experiments, on similar lines, which in no way agree with this result.

In my experiments, drops of an aqueous solution of disulphine blue were allowed to fall into a vessel of water. The vessel had a square cross-section, side 12 in., and was 18 in. deep. The drops fell from various heights, the greatest of which was 39 ft. At this height it was found that at least 50 per cent of the drops, which weighed 0·05 gm. weight, produced vortex rings. When the drops hit the water surface, smaller drops were produced in the splash, which rose to a height of a few inches, and re-entered the water forming small vortex rings. To investigate the effect of these smaller drops more fully, drops were produced varying in diameter from 500 microns to 1½ mm. These drops were allowed to fall through distances of 2 in., 4 in. and 6 in. A number of counts was taken at these heights using drops varying in size between the above limits. In every case the percentage number of drops forming vortex rings exceeded 70. From these results it seems that Reynolds's explanation of the calming of the sea by rain may be the correct one. If we regard the rain as consisting of drops hitting the sea at their terminal velocity and producing smaller drops by splashing, then the total number of drops, large and small, which produce vortex rings will be considerable—in fact, more than 50 per cent of the actual raindrops, and more than 70 per cent of the 'splash-drops'.

In the experiment, the vortex rings of the large drops falling through 39 ft. frequently travelled to the bottom of the tank with a velocity which indicated that they would have gone much farther had the tank been deeper. Although the vortex rings of the smaller drops did not travel so far, they would certainly transfer momentum from the surface to lower regions, thereby having a calming effect on the surface.

Other experiments were carried out, using various combinations of drop-size and height. As the above results have most bearing on the point at issue, a complete statistical report giving all the results seems superfluous.

C. F. Barnaby

"Harroway Villa",
Penton,
Andover, Hants.
Aug. 29.

A Method for Staining the Cuticular Lattice of *Paramecium*

Von Gelei's Toluidin Blue technique[1] yields beautifully stained preparations of the cuticular lattice of *Paramecium*, but considerable experience is required before satisfactory results are obtained, and the method takes so long (five hours) that it is of little use for class purposes. Adequate staining of the lattice can be obtained, however, by treating Schaudinn-fixed films of *Paramecium* with Giemsa's stain.

Drops of a thick culture of *Paramecium* are pipetted on to slides covered with a thin film of albumen. When the *Paramecium* film is nearly dry, the slide is placed for fifteen minutes, film face upwards, in a covered dish containing Schaudinn's fixative. The slides are then transferred through 50 and 70 to 90 per cent alcohol, where they can be stored until required. Omission of iodine treatment does not affect the preparations. The slides for staining are transferred to water, drained, and then stained for 15–20 min. with a 2·5 per cent solution of Giemsa's stain in distilled water, washed in tap water, dried in air, and examined without a coverslip under oil immersion.

While the staining of the lattice by this method is not so clear as in preparations made by von Gelei's

ethod, it enables students to demonstrate rapidly r themselves the structure of the cuticle.

C. H. Brown

Cancer Research Department,
London Hospital Medical College,
London, E.1.
July 19.

elel, J. von, *Microkosmos*, **20**, 97 (1927).

Pedogenic Inertia : a Concept in Soil Science

The purpose of this note is to direct attention to a concept in soil science for which we propose the erm 'pedogenic inertia'. This is the concept that a rocess in soil formation, once established, may con-nue in spite of changes in the environment to onditions which apparently are not normally favour-ble to this process. The argument may be stated s follows.

(1) Initially, all soils are directly related to their espective environments in which the factors of parent aterial and climate, in particular, are important. 2) Variation in parent material results in initial iversity in the soils produced under a given climate. 3) Nevertheless, any climate, if it persists unchanged, ill bring about convergence of the initially diverse oils towards one type of soil normal for that climate. 4) In the case of a change of climate, soils inherited om the earlier climate will at first differ from those rmed *ab initio* from similar parent material under he new climate. (5) Under the regime of the new limate, those changes imposed on the old soils hould, and usually do, bring about progressive con-ergence with the new soils. (6) In some notable ases this expected convergence does not take place. The old soil remains radically different from the new, even where both were developed from the same parent material. (7) In some such cases the failure to exhibit convergence is, we suggest, due to the tendency of certain well-established soil processes not merely to be passively inert to the new climatic conditions, but even to continue actively in spite of them. (8) For this property we propose the term 'pedogenic inertia'. (9) In addition to resisting convergence, pedogenic inertia may actively lead to increasing divergence. For example, under climatic conditions almost equally favourable to the development of two alternative soil types, an apparently trivial variation in the other conditions, such as drainage or slope, might result in the initiation of the two alternative soil-forming processes side by side on the same parent material. In such a case, pedogenic inertia might bring about increasing divergence in the two soils thus contemporaneously produced.

The conclusions arrived at are based on our studies of basaltic soils in eastern Australia where, over uniform parent material and on similar degrees of slope, red and black soils are commonly found side by side. The red soils are pedalferric, with kaolinitic clay and sesquioxides in the colloidal fraction, and are characteristically deep, often very deep. In contrast, the black soils give no evidence of being pedalferric or of showing a similar distribution of sesquioxides ; they are usually shallow, often stony, and the clay belongs to the montmorillonite–beidellite group. Deeper profiles commonly contain calcium carbonate in the subsoil.

Our hypothesis is that, in such cases, the red soils were initially developed under an earlier, wetter climate, and that, as a result of pedogenic inertia, such soils have persisted, little changed, in spite of a period of lowered rainfall under which the black soils were produced directly from the parent basalt where such had been exposed by erosion of the red soils.

In this particular case, we suggest that the soil-forming processes giving rise to clay minerals of the kaolinitic type in the red soils, once well established, continued under other climatic conditions where the appropriate processes would have given rise to black montmorillonitic clay soils and, indeed, did so where they acted upon fresh parent material.

An additional example is given by some of the heavy, black basaltic soils themselves, which occur in areas where the present rainfall is excessive for the production of such soils, and where the soils most recently derived from the basalt are brown soils of lighter texture and different structure. It appears that, although in this case the climatic change was a relatively recent one, the processes involved in the formation of black soils, once established, may prove to be equally persistent and thus form an equally good example of pedogenic inertia.

We submit that the postulate here presented, which in some ways may be regarded as complementary to the idea of polygenesis, may prove equally useful in the clarification and interpretation of some of the puzzling patterns in soil distribution which have long defied satisfactory explanation.

W. H. Bryan
L. J. H. Teakle

Department of Geology and
Department of Agriculture,
University of Queensland,
Brisbane.
July 6.

Spacing and 'Bolting' of Vegetables

Landau[1] has pointed out that the incidence of bolting in onions is affected by the spacing of the plants. He found that more bolting occurred on the outside rows of experimental plots than in the centre, and suggested that competition for light constituted one of the determining factors. That this effect of spacing on bolting is not an isolated phenomenon is shown by results which our experiments over a period of two years have yielded. In these experiments on beet, carrots and shallots the plant spacings have been deliberately altered by varying either the thinning or planting distance, and some of the results obtained are tabulated below. The rows of beet and carrots were in all cases 18 in. distant.

Crimson Globe Beet. 1948		Early Wonder Carrots. 1940		Early Nantes Carrots. 1949		Altrincham Carrots. 1949	
No. of plants per ft. of row	% of bolters	No. of plants per ft. of row	% of bolters	No. of plants per ft. of row	% of bolters	No. of plants per ft. of row	% of bolters
5·83	1·14	8·14	7·2	10·00	0·14	11·3	1·6
4·25	1·37	5·26	7·4	5·93	0·60	6·7	3·3
3·33	1·50	4·14	7·8	3·71	0·58	4·4	3·9
2·67	1·56	3·21	10·8	2·86	0·50	2·6	4·1
2·17	3·46	2·29	12·6				

Results of this type are not always obtained. Thus, an experiment with Altrincham carrots in 1948, in which the incidence of bolting was heavy (varying from 32 to 34 per cent), showed no relation between

spacing and bolting; but at the time when the observations were made, it is thought that all potential bolters had, in fact, bolted. With shallots grown at three inter-row distances (8, 12 and 16 in.) and four inter-plant distances (3, 6, 9 and 12 in.) the number of flower heads produced per plant was influenced by the spacing, the figures being 0·70, 0·89 and 1·09 for the 8, 12 and 16 in. rows, and 0·72, 0·90, 0·95 and 0·99 for the 3, 6, 9 and 12 in. inter-plant distances. None of the results obtained contradicts the thesis that wide spacing increases the incidence or accelerates the occurrence of bolting.

We do not, however, interpret these results as being determined by direct competition for light; but incline to the view that wider spacing allows of more rapid growth, so that with the shallots more flower heads will have emerged before, probably, lengthening days suppress further emergence, while in the root crops, on any date when bolting is progressing a greater proportion of the potential bolters will have actually bolted on the widely spaced than on the closely spaced plots. This effect will not be evident if at the time of the observation all potential bolters have, in fact, bolted, as with the Altrincham carrots in 1948.

L. G. G. Warne

Botany Department,
University,
Manchester.
Oct. 27.

[1] *Nature*, **164**, 496 (1949).

Zinc and Plant Respiration

Dufrenoy and Reed[1], in their study of coacervation in hypoplastic cells, demonstrated some important correlations with the respiratory activities in vacuoles, and they also suggested that a similar correlation between dwarfed shoots and coacervation was shown as the result of zinc deficiency in apricots and walnuts[2]. However, the effect of zinc on the respiration of plants has not hitherto been described. It is possible to determine the relationship between zinc and respiration by direct measurements of oxygen uptake and carbon dioxide evolution by the normal and zinc-deficient plants.

Oxygen uptake and carbon dioxide evolution by zinc-deficient and normal tomato leaf sections suspended in phosphate buffer, *p*H 5·0, temperature 30° C.

Plant	Length of stem (cm.)	Gas exchange in μl./200 mgm. leaf/hr.					
		First hour			Second hour		
		O_2	CO_2	R.Q.	O_2	CO_2	R.Q.
Control	11·5	80·8	113·6	1·41	75·2	100·4	1·33
−Zn	9·8	92·8	121·4	1·31	78·1	101·9	1·30
Control	28·5	81·5	109·2	1·34	87·0	119·2	1·36
−Zn	10·4	88·4	89·9	1·01	89·1	89·9	1·00
Control	35·0	86·3	95·1	1·10	76·3	85·8	1·12
−Zn	10·5	92·0	99·3	1·07	82·5	90·2	1·09

Tomato plants, *Lycopersicon esculentum* Mill. variety John Baer, were used as experimental material. The methods of culturing the plants have been described in a previous paper[3]. Gas-exchange measurements were made in Warburg's respirometer. Oxygen uptake was measured in vessels having concentrated potassium hydroxide in the central well, while the difference between oxygen uptake and carbon dioxide evolution was measured in a second vessel without potassium hydroxide in the usual way. The experiments were carried out at 30° C. Tomato leaves of normal and zinc-deficient plants were cut into pieces about 2–4 mm.^{2} in area; 200 mgm. samples were weighed out for each vessel, which contained 2 ml. of phosphate buffer of *p*H 5·0.

No significant difference in the rate of oxygen consumption and carbon dioxide evolution between the normal and zinc-deficient plants has been demonstrated. The high respiratory quotient was obtained in the early stage of growth; this is presumably due to the high organic acid content in the young plants. The results (see table) show that the rate of respiration of the zinc-deficient plants was slightly higher than that of the control: this is because the calculation is based on the fresh weight. I have already demonstrated that the zinc-deficient plant has a lower water content[4]. From the results described above, it is concluded that zinc plays no direct part in the respiratory system of the higher plants.

Cheng Tsui

Botany Department,
University of Wisconsin.

[1] Dufrenoy, J., and Reed, H. S., *Plant Physiol.*, **21**, 416 (1946).
[2] Reed, H. S., and Dufrenoy, J., *Amer. J. Bot.*, **29**, 544 (1942).
[3] Tsui, C., *Amer. J. Bot.*, **35**, 172 (1948).
[4] Tsui, C., *Amer. J. Bot.*, **35**, 309 (1948).

Occurrence of the Spiny Dog-fish *Oxynotus centrina* in South African Waters

A specimen, 22 in. in length, of *Oxynotus centrina* (Linn.) was recently trawled in 60 fathoms off the west coast of the Cape Peninsula. It is the first record of this genus in South African waters.

Although some elements of the fauna of the deep water off the Cape Peninsula show resemblances to the southern Australian fauna, there is no question of this specimen belonging to the species *bruniensis* (Ogilby). It has all the characters of the Mediterranean species[1], except the colour, which is black instead of brownish.

K. H. Barnard

South African Museum,
Cape Town.
May 18.

[1] See Norman, *Proc. Zool. Soc.*, 77 (1932).

Unicellular Algæ in Association with Invertebrates

The presence of unicellular algæ in association with a large number of invertebrate animals is well known. It occurs among members of the Protozoa, Porifera, Cœlenterata, Ctenophora, Turbellaria, Rotifera, Gastropoda and Lamellibranchiata (Yonge[1]). To this list must now be added the Brachiopoda, for I have found that in *Lingula*, growing in 0–1 fathom off Trincomalee, zooxanthellæ are abundantly present within the cells of the digestive glands. Here then is another animal digesting intracellularly and harbouring a unicellular green alga within its tissues. It is hoped to publish a fuller account of this elsewhere.

P. Kirtisinghe

Department of Zoology,
University of Ceylon,
Colombo.
July 2.

[1] Yonge, C. M., *Nature*, **134**, 12 (1934).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Saturday, December 3

LONDON COUNTY COUNCIL (at the Horniman Museum, London Road, Forest Hill, London, S.E.23), at 3.30 p.m.—Mr. A. Robinson: "Adventures in the Wye Valley".*

Monday, December 5

ROYAL GEOGRAPHICAL SOCIETY (at Kensington Gore, London, S.W.7), at 5 p.m.—Mr. F. H. W. Green: "The Value of Transport Services in the Delimitation of Town and Country".

SOCIETY OF ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Dr. H. G. Taylor: "Welding Research and Practice in the U.S.A.".

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. G. L. Brown, F.R.S.: "Chance and Design in Physiological Research" (Inaugural Lecture).*

INSTITUTION OF ELECTRICAL ENGINEERS, SOUTH MIDLAND CENTRE (at the Town Hall, Birmingham), at 6 p.m.—Dr. R. A. Smith: "Radar" (Faraday Lecture).

ROYAL INSTITUTE OF CHEMISTRY, LONDON AND SOUTH-EASTERN COUNTIES SECTION (joint meeting with the SOCIETY OF CHEMICAL INDUSTRY, at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1), at 6.30 p.m.—Mr. A. M. Robertson: "Fibreglass".

INSTITUTION OF ELECTRICAL ENGINEERS (at the Great Western Hotel, Reading), at 7 p.m.—Mr. C. A. Cameron Brown: "The Development of Electro-Horticulture".

Tuesday, December 6

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Mr. L. C. Hector: "Fashions in Forgery".*

SOCIETY OF PUBLIC ANALYSTS AND OTHER ANALYTICAL CHEMISTS (joint meeting with the FOOD GROUP of the SOCIETY OF CHEMICAL INDUSTRY, at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 3.45 p.m.—Discussion on "Properties of Pectin and its Use in the Food Industry".

EUGENICS SOCIETY (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Dr. L. F. Richardson, F.R.S.: "War and Eugenics".*

SOCIETY OF CHEMICAL INDUSTRY, CHEMICAL ENGINEERING GROUP (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. K. R. Butlin and Mr. W. H. J. Vernon: "The Underground Corrosion of Ferrous Metals in the Light of Recent Research".

INSTITUTION OF ELECTRICAL ENGINEERS, NORTH-WESTERN CENTRE (at the Engineers' Club, Albert Square, Manchester), at 6.15 p.m.—Prof. G. W. O. Howe: "Some Electromagnetic Problems".

MANCHESTER GEOGRAPHICAL SOCIETY (at the Geographical Hall, 16 St. Mary's Parsonage, Manchester), at 6.30 p.m.—Mr. W. L. Flinn: "Iran in War Time".

INSTITUTE OF PHYSICS, SCOTTISH BRANCH (at the University, Glasgow), at 7 p.m.—Prof. N. F. Mott, F.R.S.: "The Physical Strength of Metals".

WOMEN'S ENGINEERING SOCIETY (at 35 Grosvenor Place, London, S.W.1), at 7 p.m.—Discussion on "Women and Electrical Engineering".

ROYAL STATISTICAL SOCIETY, TEES-SIDE SUB-GROUP OF THE INDUSTRIAL APPLICATIONS SECTION (at the William Newton School, Norton), at 7.15 p.m.—Mr. G. E. P. Box: "Experimental Design".

Wednesday, December 7

PHYSICAL SOCIETY, COLOUR GROUP (at the E.L.M.A. Lighting Service Bureau, 2 Savoy Hill, London, W.C.2), at 3.30 p.m.—Dr. H. B. Cott: "Camouflage".

PHYSICAL SOCIETY, LOW TEMPERATURE GROUP (in the Main Physics Lecture Theatre, Imperial College of Science and Technology, Imperial Institute Road, London, S.W.7), at 5 p.m.—Fourth Annual General Meeting; at 5.30 p.m.—"The Design of Helium Liquefiers".

INSTITUTION OF ELECTRICAL ENGINEERS, RADIO SECTION (at Savoy Place, Victoria Embankment, London, W.C.2), at 5.30 p.m.—Dr. J. L. Pawsey: "Solar Radio-Frequency Radiation" (Paper to be read by Mr. J. S. Hey).

MANCHESTER METALLURGICAL SOCIETY (at the Engineers' Club, Albert Square, Manchester), at 6.30 p.m.—Mr. N. Davidson: "Design of Wire Drawing and other Cold Working Machines".

BRITISH INSTITUTION OF RADIO ENGINEERS, MERSEYSIDE SECTION (at the Accountants' Hall, Derby Square, Liverpool), at 7 p.m.—Dr. J. D. Craggs: "The Acceleration of Atomic Particles to High Energies".

INSTITUTE OF WELDING, MANCHESTER AND DISTRICT BRANCH (in the Reynolds Hall, College of Technology, Manchester), at 7 p.m.—Mr. C. C. Henderson: "Stud Welding".

Thursday, December 8

INSTITUTION OF WORKS MANAGERS, WEMBLEY SUB-BRANCH (at the Rest Hotel, Kenton), at 12.30 p.m.—Mr. L. E. Johnson: "Manpower and Industrial Output".

CHADWICK PUBLIC LECTURE (at St. Mary's Hospital Medical School, Norfolk Place, Praed Street, London, W.2), at 4.30 p.m.—Dr. G. B. Dowling: "Generalized Systemic Sclerosis (Progressive Symmetrical Scleroderma-Dermatomyositis)" (Malcolm Morris Memorial Lecture).*

INSTITUTE OF PHYSICS (at 47 Belgrave Square, London, S.W.1), at 5.30 p.m.—Dr. F. P. Bowden: "Some Physical and Chemical Effects of Friction".

INSTITUTION OF THE RUBBER INDUSTRY, LEICESTER SECTION (at the Bell Hotel, Leicester), at 7.30 p.m.—Debate on "Technical Progress is in the Hands of Individual Firms".

PHARMACEUTICAL SOCIETY (at 17 Bloomsbury Square, London, W.C.1), at 7.30 p.m.—Mr. E. C. Cripps: "Pharmacy in the Eighteenth and Early Years of the Nineteenth Century".

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place, London, W.1), at 7.30 p.m.—Mr. C. J. Moss: "Bonding of Aircraft Materials with Synthetic Adhesives".

Friday, December 9

ROYAL ASTRONOMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Scientific Papers.

INSTITUTION OF WORKS MANAGERS, MANCHESTER BRANCH (at the Engineers' Club, Albert Square, Manchester), at 6.30 p.m.—Prof. R. E. Lane: "Occupation and Health".

MANCHESTER STATISTICAL SOCIETY, INDUSTRIAL GROUP (at the Albert Hall, Peter Street, Manchester), at 6.45 p.m.—Mr. G. E. P. Box: "The Design and Analysis of a Chemical Experiment".

INSTITUTE OF PHYSICS, MANCHESTER AND DISTRICT BRANCH (in the New Physics Theatre, The University, Manchester), at 7 p.m.—Prof. P. M. S. Blackett, F.R.S.: "Fundamental Particles of Nature".

ROYAL STATISTICAL SOCIETY, SOUTH WALES GROUP of the INDUSTRIAL APPLICATIONS SECTION (at the South Wales Electricity Board Show Rooms, Newport, Mon.), at 7 p.m.—Dr. J. C. P. Miller: "The Use of Calculating Machines in Statistical Computing".

SOCIETY OF CHEMICAL INDUSTRY, FINE CHEMICALS GROUP (in the Chemistry Lecture Theatre, King's College, Strand, London, W.C.2), at 7 p.m.—Dr. B. A. Hems: "A Synthesis of L-Thyroxine".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. M. G. Evans, F.R.S.: "Oxidation-Reduction Reactions".

Saturday, December 10

PHYSICAL SOCIETY (in the Physics Department, The University, Edgbaston, Birmingham), at 9.30 a.m.—Autumn Provincial Meeting on "Nuclear Physics".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER IN ELECTRICAL ENGINEERING, and LECTURERS (2) IN MATHEMATICS AND PHYSICS—The Secretary, South-East London Technical College, Lewisham Way, London, S.E.4 (December 9).

PATENT EXAMINERS (with an honours degree in physics, chemistry, electrical engineering or mechanical engineering, or an equivalent qualification) in the Board of Trade, the Admiralty, and the Ministry of Supply—The Secretary, Civil Service Commission, 6 Burlington Gardens, London, W.1, quoting No. 2866 (December 10).

SCIENTIFIC OFFICER IN THE NUTRITION DEPARTMENT, to work on problems of animal nutrition, including those connected with the biological assay of vitamins and other factors—The Secretary, National Institute for Research in Dairying, Shinfield, Reading, Berks (December 10).

CHEMICAL ENGINEERS (Principal Scientific Officer or Senior Scientific Officer grade) at a Ministry of Supply research establishment in London area—The Technical and Scientific Register (K), York House, Kingsway, London, W.C.2, quoting F.814/49BN (December 14).

READER IN GEOLOGY—The Registrar, University College of North Staffordshire, c/o Town Clerk, Stoke-on-Trent (December 15).

PHYSICISTS (Senior Scientific Officer grade) at the Royal Aircraft Establishment, Farnborough, for theoretical investigation concerned with the basic principles of weapon design—The Technical and Scientific Register (K), York House, Kingsway, London, W.C.2, quoting A.282/49BN (December 16).

SENIOR RESEARCH OFFICERS OR RESEARCH OFFICERS, DIVISION OF ENTOMOLOGY, Canberra (Appointment No. 2503), a SENIOR RESEARCH OFFICER or RESEARCH OFFICER, DIVISION OF FOREST PRODUCTS, Melbourne (Appointment No. 2504), a RESEARCH OFFICER, CEMENT AND CERAMICS SECTION, DIVISION OF INDUSTRIAL CHEMISTRY, Melbourne (Appointment No. 2505), a RESEARCH OFFICER, POLAROGRAPHIC RESEARCH, DIVISION OF INDUSTRIAL CHEMISTRY, Melbourne (Appointment No. 2506)—The Chief Scientific Liaison Officer, Australian Scientific Research Liaison Office, Africa House, Kingsway, London, W.C.2, quoting the appropriate Appointment No. (December 24).

SCIENTIST, Grade III (with a University honours degree in chemistry or the equivalent, and preferably with some knowledge of fuel technology or an allied subject) in the Scientific Department at London headquarters—The National Coal Board, Establishments (General) Branch, Hobart House, Grosvenor Place, London, S.W.1, quoting TT.168 (December 24).

VEGETABLE RESEARCH OFFICER, AGRONOMY DIVISION, Scientific and Industrial Research Department, Lincoln, N.Z.—The Office of the High Commissioner for New Zealand, 415 Strand, London, W.C.2 (December 30).

PROFESSOR OF GEOLOGY in Auckland University College (University of New Zealand)—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (December 31).

SENIOR LECTURER (or ASSOCIATE PROFESSOR) IN PHYSIOLOGY OF DOMESTIC ANIMALS, and a SENIOR LECTURER IN AGRICULTURAL BIOCHEMISTRY, in the University of Melbourne—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (December 31).

LECTURER IN ZOOLOGY in Rhodes University College, Grahamstown, South Africa—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (December 31).

TRAINED ANALYST to take charge of regular chemical analyses of water samples—The Director, Freshwater Biological Association, Wray Castle, Ambleside, Westmorland (December 31).

ASSISTANT PROFESSOR OF THEORETICAL PHYSICS—Prof. J. K. Robertson, Queen's University, Kingston, Ont., Canada (January 10).

LECTURER IN APPLIED MATHEMATICS (preferably with an interest in Mathematical Physics), and a LECTURER IN CHEMISTRY (with experience in Physical Chemistry), in the University of Otago, Dunedin —The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (January 31).

PROFESSOR OF MECHANICAL ENGINEERING, and a PROFESSOR OF PHILOSOPHY, in the University of the Witwatersrand, Johannesburg, —The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (January 31).

PROFESSOR OF PHILOSOPHY, a PROFESSOR and a LECTURER IN MATHEMATICAL PHYSICS, a READER and a SENIOR LECTURER IN MATHEMATICS, a SENIOR LECTURER and LECTURERS (2) IN PHYSICS, a SENIOR LECTURER IN INORGANIC AND PHYSICAL CHEMISTRY, a READER IN BOTANY, a SENIOR LECTURER IN PALÆONTOLOGY, a SENIOR LECTURER and a LECTURER IN PHYSIOLOGY, a SENIOR LECTURER IN ANATOMY, a SENIOR LECTURER IN PATHOLOGY, a SENIOR LECTURER IN MECHANICAL ENGINEERING (preferably in Fluid Mechanics), a SENIOR LECTURER IN CIVIL ENGINEERING, a SENIOR LECTURER IN MINING AND METALLURGY, a LECTURER IN ELECTRICAL ENGINEERING, a READER IN PSYCHOLOGY, and a LECTURER IN PHILOSOPHY, in the University of Adelaide—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (January 31).

EDWARD A. DEEDS FELLOWSHIP in University College, Dundee, for research in Physical Science (Engineering, Metallurgy, Chemistry, Physics, Mathematical Physics, or any cognate subject)—The Secretary, University College, Dundee (March 31).

PLANT PATHOLOGIST in the Agricultural Department, Kenya—The Director of Recruitment, Colonial Office, Sanctuary Buildings, Great Smith Street, London, S.W.1.

ENTOMOLOGIST in a Filariasis Research Unit in East Africa—The Under-Secretary of State, Colonial Office, Research Department, Sanctuary Buildings, Great Smith Street, London, S.W.1.

LECTURER IN CHEMISTRY (to teach to Intermediate and Final B.Sc. degree standard)—The Clerk, Northern Polytechnic, Holloway, London, N.7.

PRINCIPAL MEDICAL OFFICER—Research (bacteriologist with good experience of original research, and recognized medical qualifications), a PRINCIPAL SCIENTIFIC OFFICER (bacteriologist with good experience of original research, and recognized qualification in veterinary science), a PRINCIPAL SCIENTIFIC OFFICER (biochemist with good honours degree and good experience of original research with special knowledge of bacterial chemistry), MEDICAL OFFICERS—Research (bacteriologists or experimental pathologists with experience of original research, and recognized medical qualifications), SENIOR SCIENTIFIC OFFICERS (bacteriologists with experience of original research, and recognized qualification in veterinary science), SENIOR SCIENTIFIC OFFICERS (biochemists with good honours degree and research experience in bacterial chemistry), EXPERIMENTAL OFFICERS (highly skilled in experimental bacteriology), at a Ministry of Supply Research Establishment in S. England—The Secretary, Civil Service Commission, Scientific Branch, 27 Grosvenor Square, London, W.1, quoting No. 2729.

GRADUATE CHEMIST (preferably with an honours degree) for work, mainly analytical, dealing with the serviceability of a wide range of shoe materials and their suitability for shoe manufacturing processes—The Director, British Boot, Shoe and Allied Trades Research Association, Satra House, Rockingham Road, Kettering.

PRINCIPAL OF THE SOUTH-EAST ESSEX TECHNICAL COLLEGE AND SCHOOL OF ART—The Acting Chief Education Officer, County Offices, Chelmsford, Essex.

PHYSICIST TO THE REGIONAL RADIUM CENTRE, North Staffordshire Royal Infirmary—The Secretary, Hospital Management Committee, Stoke-on-Trent.

SENIOR TECHNICIAN OR LABORATORY STEWARD IN THE DEPARTMENT OF GEOLOGY—The Bursar, The University, Western Bank, Sheffield 10.

I.C.I. RESEARCH FELLOWSHIPS IN BIOCHEMISTRY, CHEMISTRY, ENGINEERING, PHARMACOLOGY OR PHYSICS—The Secretary, The University, Edinburgh (March 1). (The address was incorrectly given as Sheffield under 'Appointments Vacant' in our issue for November 26.)

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Nuffield Foundation. Report of the Trustees for the Year ending 31 March 1949. Pp. 128. (London: Nuffield Foundation, 1949.) [168

Education, Work and Management. Report of the BACIE Annual Conference held at Ashridge, 29th October–1st November 1948. Pp. 116. (London: British Association for Commercial and Industrial Education, 1949.) 5*s*. [168

Ministry of Agriculture and Fisheries. Fishery Investigations, Series 2, Vol. 17, No. 3: The Setting Behaviour of Larvae of the European Flat Oyster, *Ostrea edulis* L., and its Influence on Methods of Cultivation and Spat Collection. By Dr. H. A. Cole and E. W. Knight Jones. Pp. 32. (London: H.M. Stationery Office, 1949.) 2*s*. net. [168

Forestry Commission. National Forest Park Guides: Glen More. Edited by Prof. John Walton. Pp. v+72. (London: H.M. Stationery Office, 1949.) 2*s*. net. [168

B.I.O.S. Overall Report No. 13: Developments in the Cotton, Rayon and Silk Industries in Germany during the Period 1939–1945. By F. Charnley, R. G. Fargher, D. W. Hill and L. H. C. Tippett. Pp. 178. 3*s*. net. B.I.O.S. Overall Report No. 14: The Food Manufacturing Industry in Germany during the Period 1939–1945. Pp. 134. 2*s*. 6*d*. net. (London: H.M. Stationery Office, 1949.) [168

Air Ministry: Meteorological Office. Geophysical Memoirs, No. 82: Weather Forecasting in Tropical Regions. By Dr. A. G. Forsdyke. (M.O. 499b.) Pp. 47. 2*s*. 6*d*. net. Geophysical Memoirs, No. 83: Wind at 100,000 feet over South-East England; Observations and a Discussion of the Monsoon Theory of Wind at Great Heights. By R. J. Murgatroyd and Dr. C. J. H. Clews. (M.O. 499c.) Pp. 14. 6*d*. net. (London: H.M. Stationery Office, 1949.) [168

Annual Report for 1948 (No. 61) of the Marine Biological Station at Port Erin, Isle of Man. Drawn up by Prof. J. H. Orton. Pp. 34. (Liverpool: University Press of Liverpool, 1949.) 3*s*. [168

Agricultural Research Council. Report Series, No. 8: The Quantitative Study of Foot-and-Mouth Disease Virus. By Dr. W. M. Henderson. Pp. ix+50+8 plates. (London: H.M. Stationery Office, 1949.) 2*s*. 6*d*. net. [168

Department of Scientific and Industrial Research. Report of the Food Investigation Board, with the Report of the Director of Food Investigation for the Year 1947. Pp. iii+22. (London: H.M. Stationery Office, 1949.) 6*d*. net. [168

British Institute of Management. Conference Series 2: Management and the Financier, by H. N. Hume; Management in Private Enterprise and Nationalized Industry, by Sir Miles Thomas. Pp. 24. (London: British Institute of Management, 1949.) 2*s*. 6*d*. [168

British Museum (Natural History): Department of Mineralogy. Guide to the Collection of Rocks. Second edition. Pp. v+42. (London: British Museum (Natural History), 1949.) 1*s*. [168

Air Ministry: Meteorological Office. Weather on the West Coast of Tropical Africa from 20° N. to 20° S. including the Atlantic Ocean to 25° W. (M.O. 492.) Pp. 282. (London: H.M. Stationery Office, 1949.) 5*s*. net. [168

International Congress on Mental Health, London 1948. Vol. 1: History, Development and Organisation. Pp. 154. 10*s*. net; 2.50 dollars. Vol. 2: Proceedings of the International Conference on Child Psychiatry, 11th–14th August. Pp. 142. 10*s*. net; 2.50 dollars. Vol. 3: Proceedings of the International Conference on Medical Psychotherapy, 11th–14th August. Pp. 129. 10*s*. net; 2.50 dollars. Vol. 4: Proceedings of the International Conference on Mental Hygiene, 16th–21st August. Pp. 330. 20*s*. net; 5 dollars. (London: H. K. Lewis and Co., Ltd.; New York: Columbia University Press, 1949.) [168

Other Countries

Anthropological Records. Vol. 4, No. 1: Culture Element Distributions, 12, Apache-Pueblo. By E. W. Gifford. Pp. vi+207. 10*s*. 6*d*. net. Vol. 10, No. 1: Yokuts and Western Mono Ethnography, 1, Tulare Lake, Southern Valley, and Central Foothill Yokuts. By A. H. Gayton. Pp. x+142. 10*s*. 6*d*. net. Vol. 10, No. 2: Yokuts and Western Mono Ethnography, 2, Northern Foothill Yokuts and Western Mono. By A. H. Gayton. Pp. x+143–301. 10*s*. 6*d*. net. (Berkeley, Calif.: University of California Press; London: Cambridge University Press, 1940–1948.) [158

Ciência e Cultura. Vol. 1, N. 1–2, Janeiro e Abril. Pp. 72. (São Paulo: Sociedade Brasileira para o Progresso da Ciência, 1949.) [158

Indian Phytopathology. Vol. 1, No. 1. Pp. 96. (New Delhi: Indian Phytopathological Society, 1949.) Annual subscription, 14 rupees; 21*s*. [158

Mémoires du Musée Royal d'Histoire Naturelle de Belgique. Mémoire No. 106: Revision des Mollusques de la Belgique, 1, Mollusques Terrestres et Dulcicoles. Par Dr. William Adam. Pp. 298+6 plates. Mémoire No. 107: Les Coelentérés de la Faune Belge; leur bibliographie et leur distribution. Par Dr. Eugène Leloup. Pp. 72. Mémoire No. 108: Étude sur les Mymarommidae et les Mymaridae de la Belgique (Hymenoptera chalcidoidea.) Par Prof. Hubert Robert Debauche. Pp. 247+24 plates. Mémoire No. 109: Contribution à l'étude des Microfossiles de l'Éocène Belge. Par Dr. André Pastiels. Pp. 77+6 plates. Mémoire No. 110: Végétaux du Dévonien supérieur de la Belgique. Par Dr. Francois Stockmans. Pp. 85+14 plates. (Bruxelles: Musée Royal d'Histoire Naturelle de Belgique, 1947–1948.) [158

Mémoires du Musée Royal d'Histoire Naturelle de Belgique, Deuxième Série. Fasc. 29: Revision d'un groupe de Colubridae africains: genres Calamelaps, Miodon, Aparallactus et formes affines. Par Gaston-Francois de Witte et Raymond Laurent. Pp. 134. Fasc. 30: Gastropodes du Miocene moyen du Bassin de la Loire, Première partie. Par Maxime Glibert. Pp. 240+12 plates. (Bruxelles: Musée Royal d'Histoire Naturelle de Belgique, 1947–1949.) [158

Colony of Trinidad and Tobago. Administration Report of the Conservator of Forests for the Year 1947. Pp. 28. (Trinidad: Forest Department, 1949.) [158

Report of the King Institute of Preventive Medicine, Guindi, for the Period from 1st April 1946 to 31st March 1947, by Dr. C. G. Pandit; and Report of the Government Analyst, Madras, by K. V. Sundaram Ayyar. Pp. 63. (Madras: Government Press, 1949.) 1.2 rupees. [158

Carlsberg Foundation's Oceanographical Expedition round the World 1928–30 and previous *Dana* Expeditions. *Dana* Report No. 32: *Vampyroteuthis infernalis* Chun, an Archaic Dibranchiate Cephalopod. 2, External Anatomy. By Grace E. Pickford. Pp. 132 (9 plates). (Copenhagen: C. A. Reitzels Forlag; London: Oxford University Press, 1949.) 20*s*. [168

American Mathematical Monthly. Vol. 56, No. 1, Part 2: Outline of the History of Mathematics. By Raymond Clare Archibald. (The Second Herbert Ellsworth Slaught Memorial Paper.) Sixth edition, revised and enlarged. Pp. iii+114. (Buffalo: Mathematical Association of America, 1949.) 1 dollar. [168

Universidad Pontificia de Comillas: Miscelanea Comillas. Humanidades. Tomo 1, Núm. 1. Pp. 142. (Comillas: Universidad Pontificia, 1949.) Subscription, 30 pesetas. [168

Transactions of the National Institute of Sciences of India. Vol. 2, No. 2: Systematics, Ecology and Bionomics of Mammals studied in connection with Tsutsugamushi Disease (Scrub Typhus) in the Assam-Burma War Theatre during 1945. By Major M. L. Roonwal. Pp. 67–122+6 plates. 10 rupees. Vol. 3, No. 3: Dykes in Western India: a Discussion of their Relationships with the Deccan Traps. By Dr. J. B. Auden. Pp. 123–157+plates 7–12. 5 rupees. (Delhi: National Institute of Sciences of India, 1949.) [168